Oncologie Thoracique

Mardi 11 Juin 2024

Le Palais de la Bourse

Rémi Veillon – CHU Bordeaux

4e Post-ASCO en Nouvelle Aquitaine : les scoops de l'ASCO 2024

Liens d'intérêts

- Participation à des congrès (ASCO, ESMO, WCLC) :
  - Pfizer, MSD, Bristol-Myers Squibb, Takeda, Regeneron, Janssen
- Board local d'experts ; animations ou interventions (réunions d'experts, post-congrès) :
  - Boehringer-Ingelheim, Roche, Astra-Zeneca, Bristol-Myers Squibb, MSD, Pfizer, Takeda, Sanofi, Janssen
- Consultant
  - MSD ; Janssen
- Honoraires investigateurs dans le cadre de recherche clinique
  - Roche, Astra-Zeneca, Takeda, Abbvie, Merck-Serono, Bristol-Myers Squibb, GSK, Novartis, Janssen, Gilead, Sanofi

Oncologie Thoracique

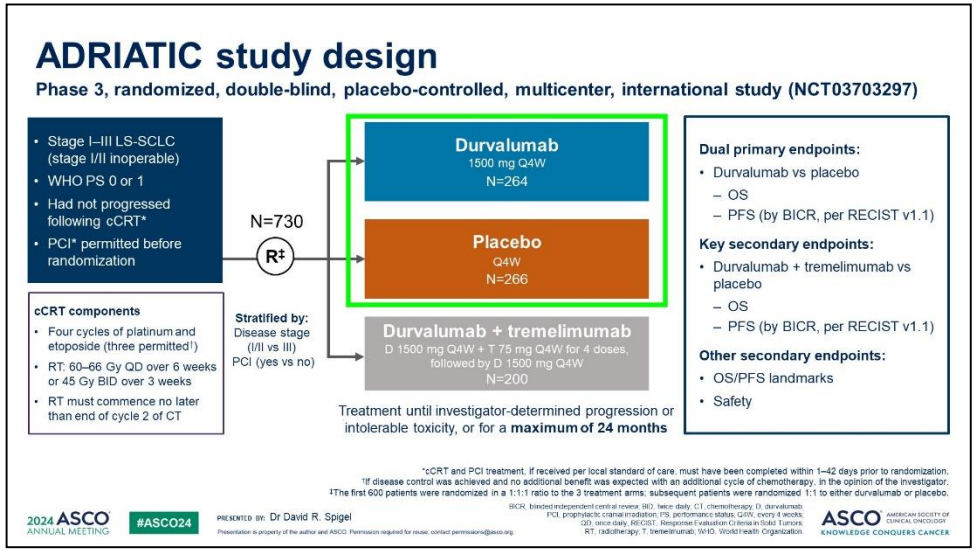
Programme

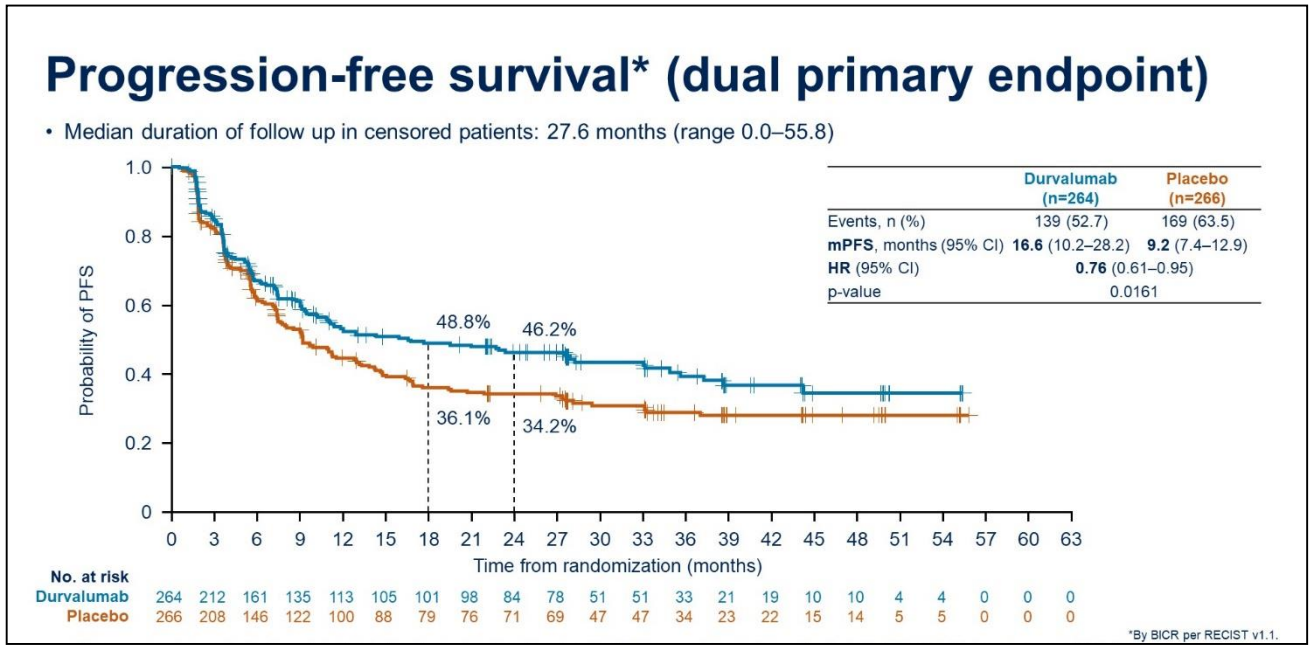
- Immunothérapie :
  - ADRIATIC : Durvalumab après Radio-chimiothérapie concomitante (CPC)
- Anticorps Conjugués (ADC)
  - Sacitizumab Govitecan ; Datopotamab deruxtecan, Sigvotatug Vedotin, Telisotuzumab Vedotin
- Addictions Oncogéniques
  - LAURA : Osimertinib après radiochimiothérapie concomitante (EGFR)
  - KRas : Adagrasib, Olomorasib, Divarasib
  - Lorlatinib (ALK/ROS)
  - Vrac : ROS1, EGFR ex20, EGFR rares, HER2/NRG1

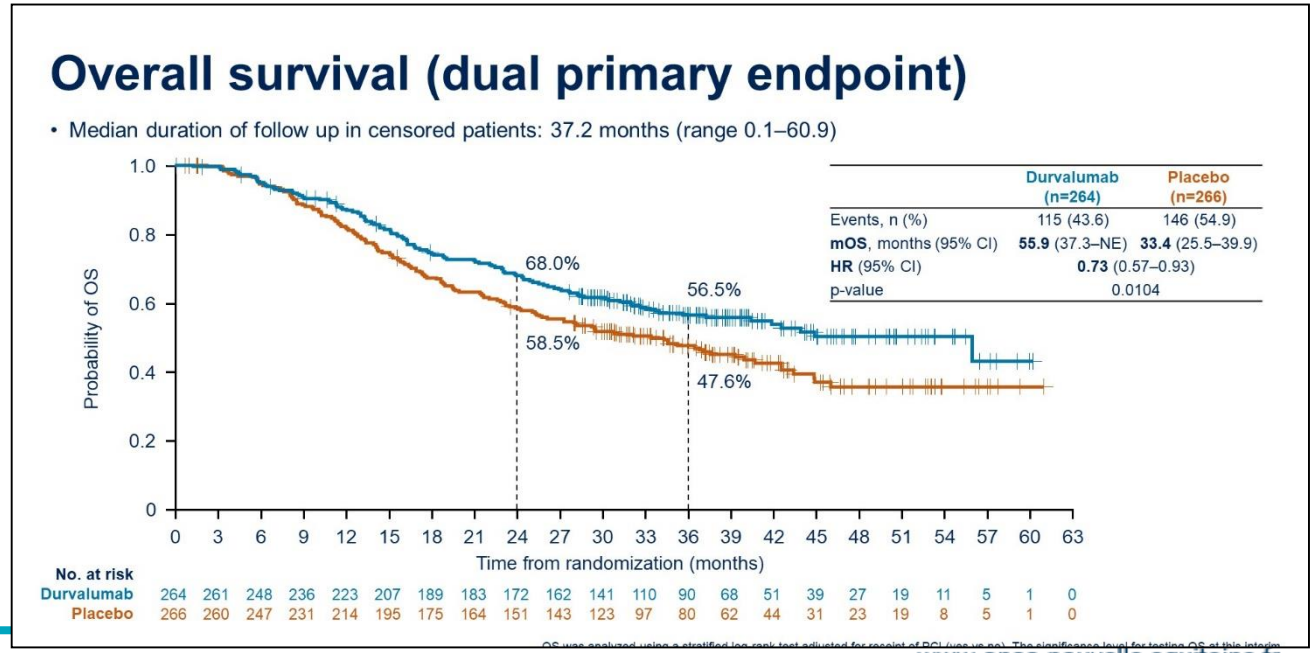
ADRIATIC

Carcinome à petites cellules :

Durvalumab après radiochimiothérapie concomitante







Spigel ; LBA5

LAURA

CBNPC muté EGFR : Osimertinib après RCC

LAURA Phase 3 double-blind study design

Patients with locally advanced, unresectable stage III[a] EGFRm NSCLC with no progression during / following definitive CRT[†] treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III[a] NSCLC
- Ex19del / L858R[‡]
- Maximum interval between last dose of CRT and randomization: 6 weeks

Osimertinib 80 mg, once daily

Randomization 2:1 (N=216)

Stratification by: Concurrent vs sequential CRT; Stage IIIA vs stage IIIB/IIIC; China vs non-China

Placebo, once daily

Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after BICR-confirmed progression offered to both treatment arms[§]

Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Endpoints
- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

[a]According to AJCC (UICC staging (8th edition).
[†]Concurrent or sequential CRT comprising ≥2 cycles of platinum-based chemotherapy (or 5 doses of weekly platinum-based chemotherapy) and a total dose of radiation of 60 Gy, ≤10%
[‡]Central or FDA-approved local testing (from a CLIA-approved laboratory, or accredited local laboratory for sites outside of USA) based on tissue
[§]If defining clinical benefit (osimertinib arm), by the judgement of treating physician (placebo arm).

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; CLIA, Clinical Laboratory Improvement Amendments; CNS, central nervous system; CRT, chemoradiotherapy; CT, computed tomography; EGFRm, epidermal growth factor receptor mutation; Ex19del, exon 19 deletion; FDA, Food and Drug Administration; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; UICC, Union for International Cancer Control; WHO PS, World Health Organization performance status

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Dr Suresh S. Ramalingam

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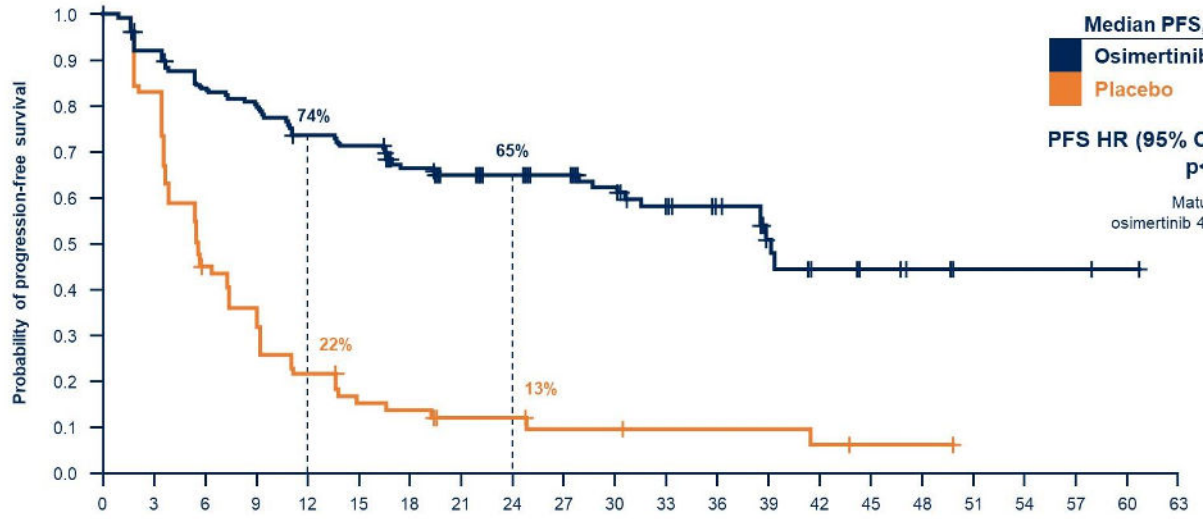
Progression-free survival by BICR



No. at risk																						
Osimertinib	143	127	114	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

Data cut-off: January 5, 2024.

Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.0 months, placebo 5.8 months. Median follow-up for PFS (censored patients): osimertinib 27.7 months, placebo 19.5 months.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

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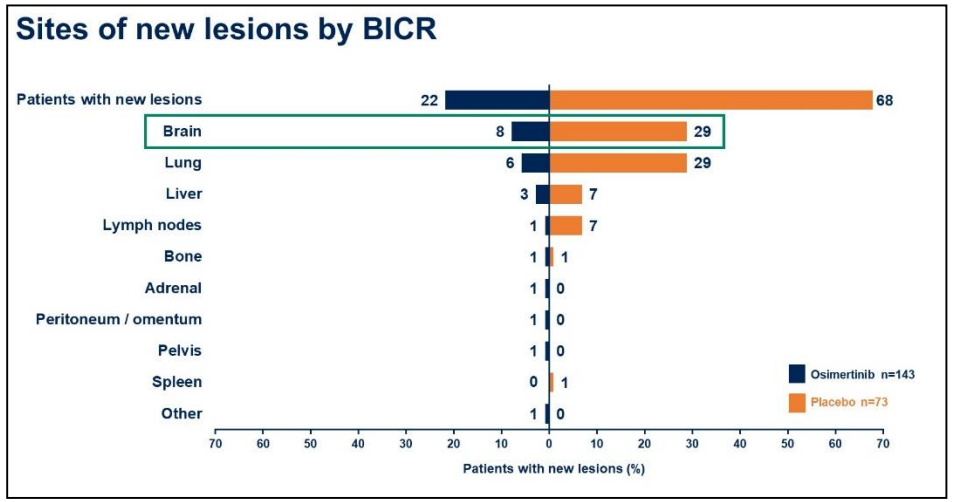
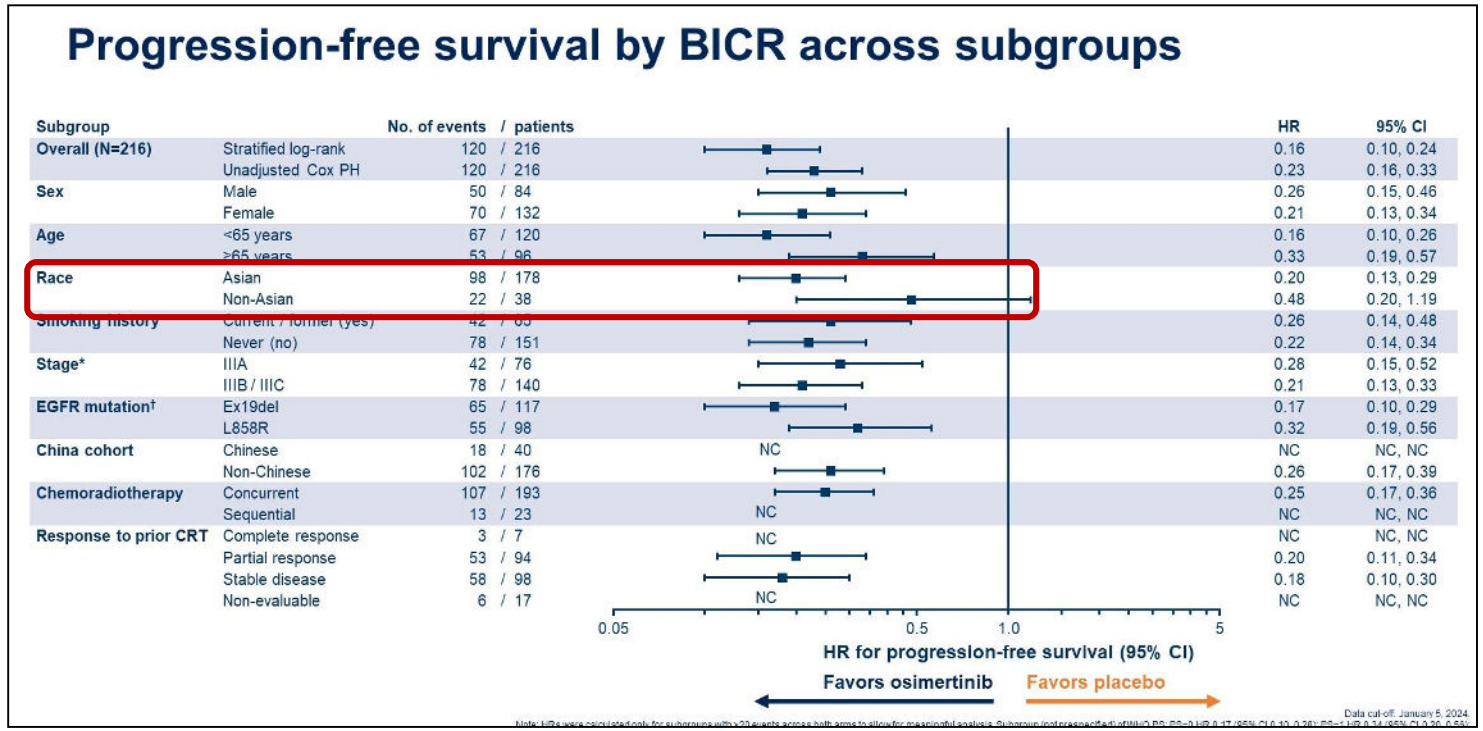
LAURA

Points forts / Points Faibles





- Survie sans progression : HR 0,16 ; 39 mois vs 5,6 mois
- Efficacité au niveau cérébral

- Bras standard extrêmement faible (5,6 mois en post-RCC)
- Population : 80% asiatique, peu de données sur le bilan initial
- Durée de traitement : à vie !

Ramalingam ; LBA4

Anticorps conjugués (ADC's)

2e ligne, vs Docetaxel

- Survie sans progression médiane de 4 mois
- Survie globale de 10 mois

- Validé vs placebo
- A l'époque le JCO est en noir&blanc…

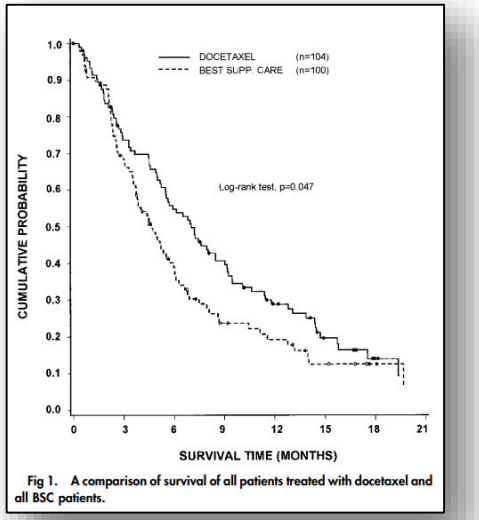
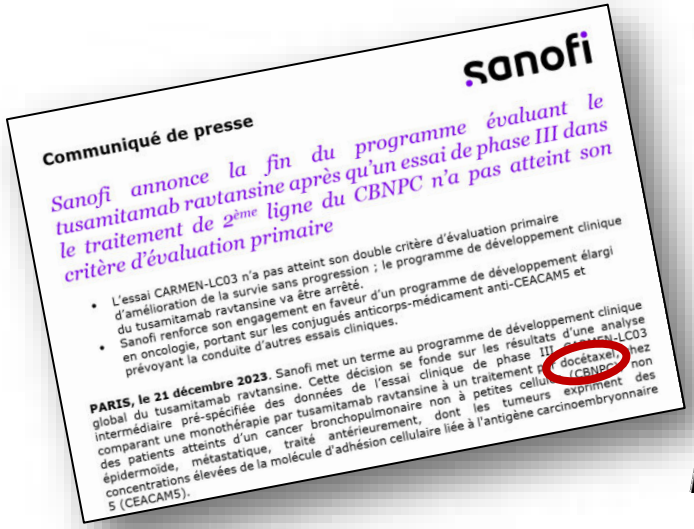


Fig 1. A comparison of survival of all patients treated with docetaxel and all BSC patients.

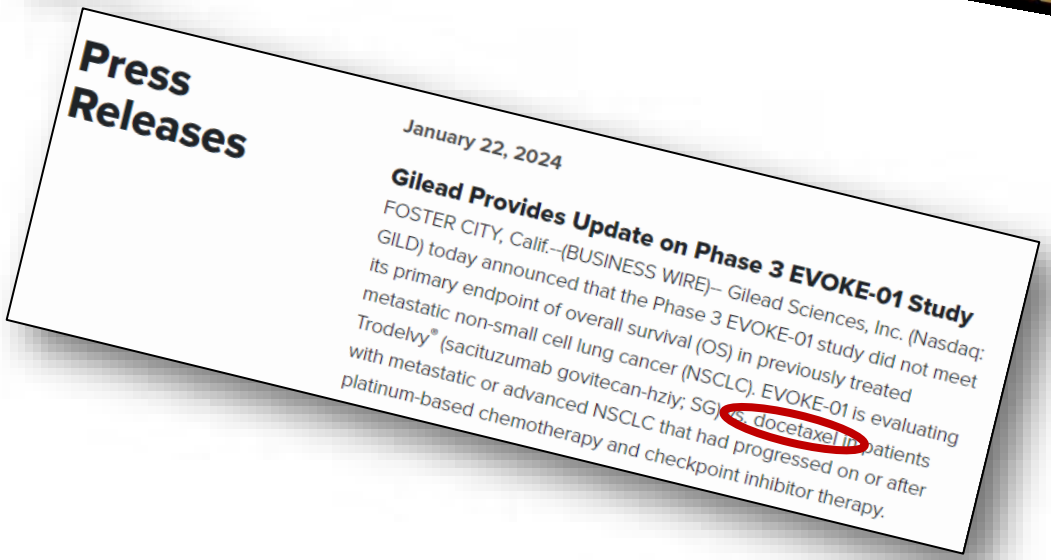

Communiqué de presse

sanofi

Sanofi annonce la fin du programme évaluant le tusamitamab ravtansine après qu'un essai de phase III dans le traitement de 2ème ligne du CBNPC n'a pas atteint son critère d'évaluation primaire

- L'essai CARMEN-LC03 n'a pas atteint son double critère d'évaluation primaire d'amélioration de la survie sans progression ; le programme de développement clinique du tusamitamab ravtansine va être arrêté.
- Sanofi renforce son engagement en faveur d'un programme de développement élargi en oncologie, portant sur les conjugués anticorps-médicament anti-CEACAM5 et prévoyant la conduite d'autres essais cliniques.

PARIS, le 21 décembre 2023. Sanofi met un terme au programme de développement clinique global du tusamitamab ravtansine. Cette décision se fonde sur les résultats d'une analyse intermédiaire pré-spécifiée des données de l'essai clinique de phase III CARMEN-LC03 comparant une monothérapie par tusamitamab ravtansine à un traitement par docétaxel, chez des patients atteints d'un cancer bronchopulmonaire non à petites cellules (CBNPC) non épidermoïde, métastatique, traité antérieurement, dont les tumeurs expriment des concentrations élevées de la molécule d'adhésion cellulaire liée à l'antigène carcinoembryonnaire 5 (CEACAM5).


Press Releases

January 22, 2024

Gilead Provides Update on Phase 3 EVOKE-01 Study

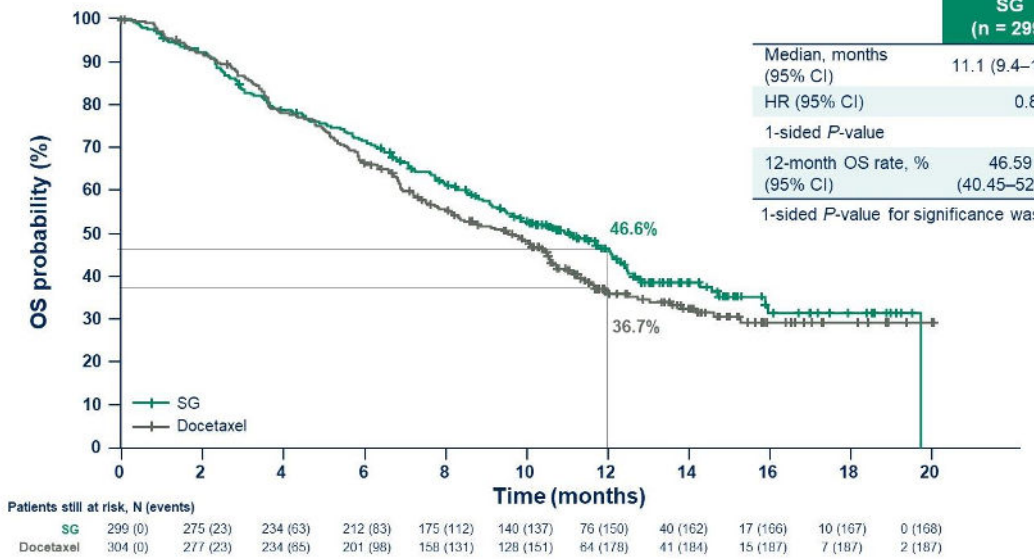
FOSTER CITY, Calif.--(BUSINESS WIRE)-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the Phase 3 EVOKE-01 study did not meet its primary endpoint of overall survival (OS) in previously treated metastatic non-small cell lung cancer (NSCLC). EVOKE-01 is evaluating Trodelvy® (sacituzumab govitecan-hziy; SG) vs. docetaxel in patients with metastatic or advanced NSCLC that had progressed on or after platinum-based chemotherapy and checkpoint inhibitor therapy.

Shepherd et al ; JCO 2000 ; 18:2095-103

Anticorps conjugués (ADC's)

Sacitizumab Govitecan (anti TROP2)

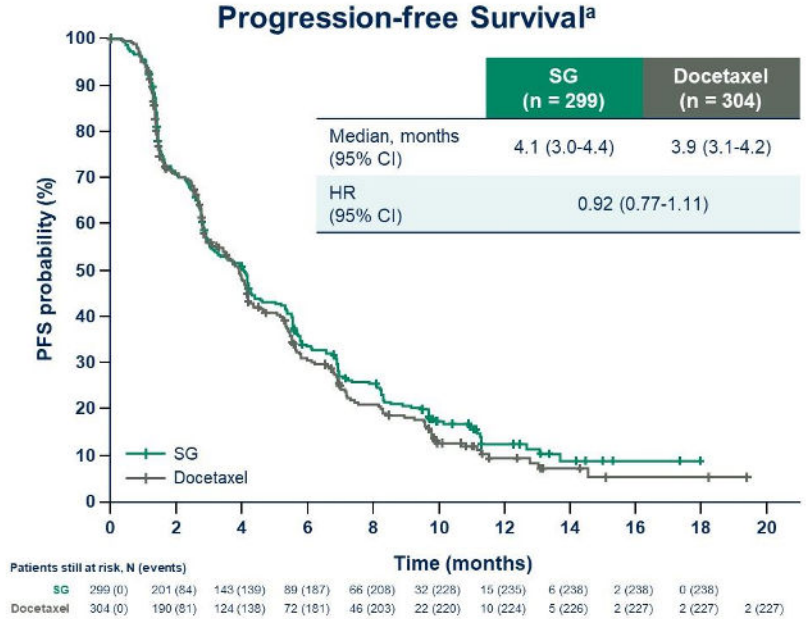
Primary End Point: Overall Survival (ITT)



	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	11.1 (9.4–12.3)	9.8 (8.1–10.6)
HR (95% CI)	0.84 (0.68–1.04)	
1-sided *P*-value	0.0534	
12-month OS rate, % (95% CI)	46.59 (40.45–52.50)	36.72 (30.88–42.57)

1-sided *P*-value for significance was $P \leq 0.0223$

Secondary End Points (ITT)



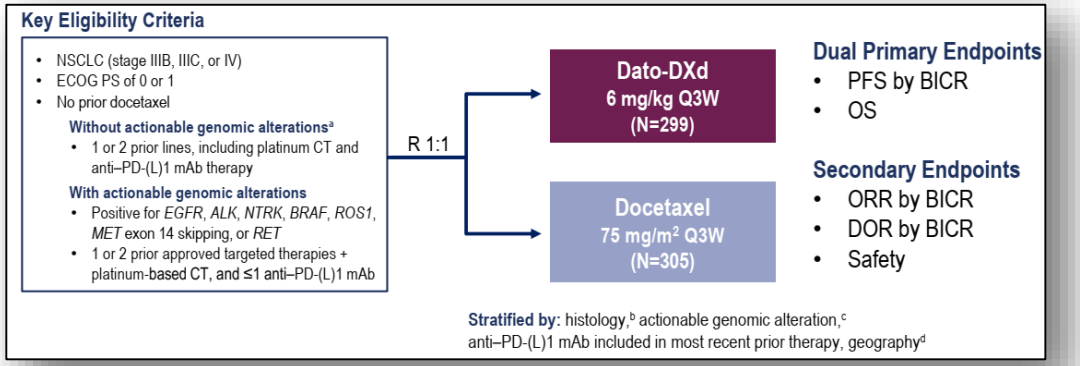
	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	4.1 (3.0-4.4)	3.9 (3.1-4.2)
HR (95% CI)	0.92 (0.77-1.11)	

Paz Ares ; LBA8500

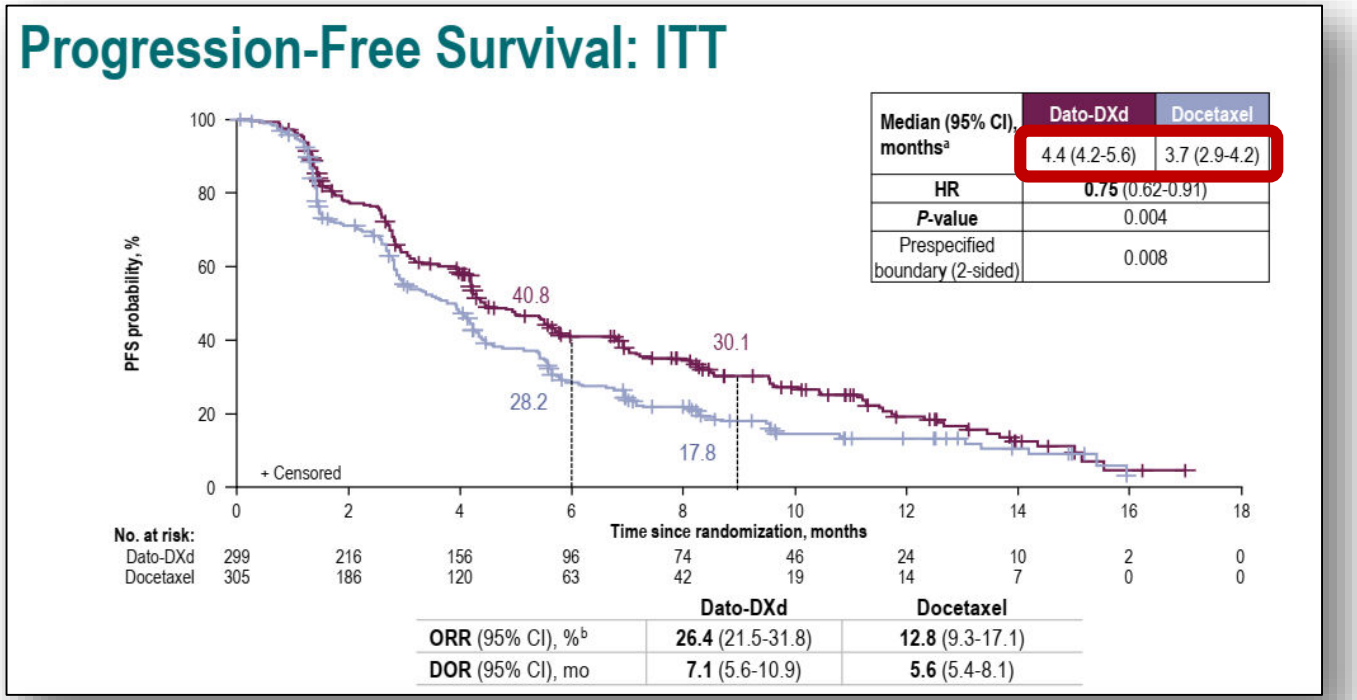
ADC's

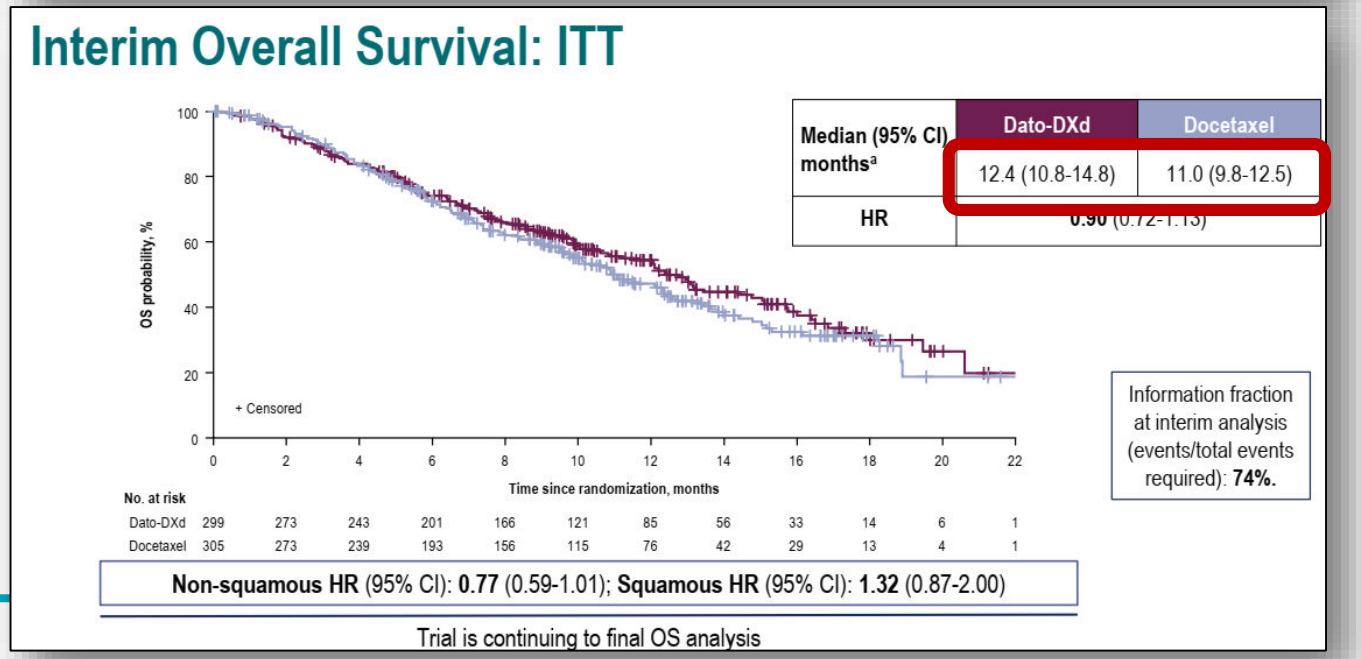
Datopotamab Deruxtecan

- Datopotamab : Anti TROP2
- Deruxtecan : Inhibiteur de Topoisomérase I



Ahn et al ESMO 2023 Abstr LBA12

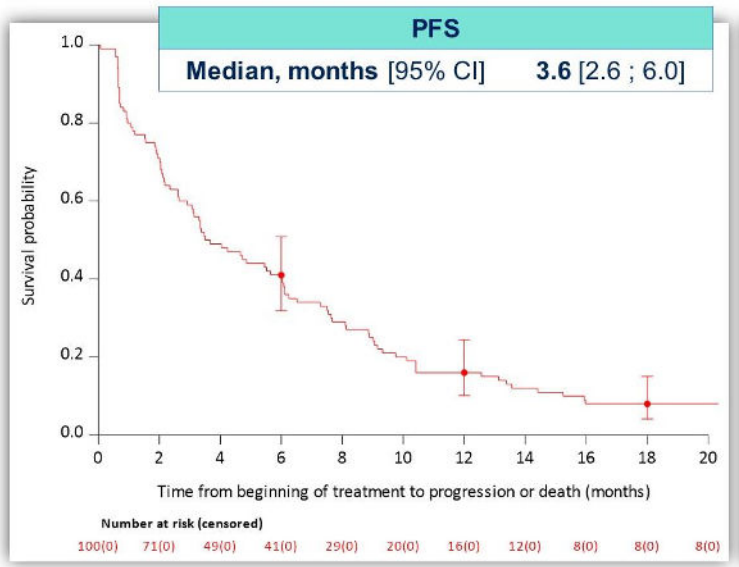


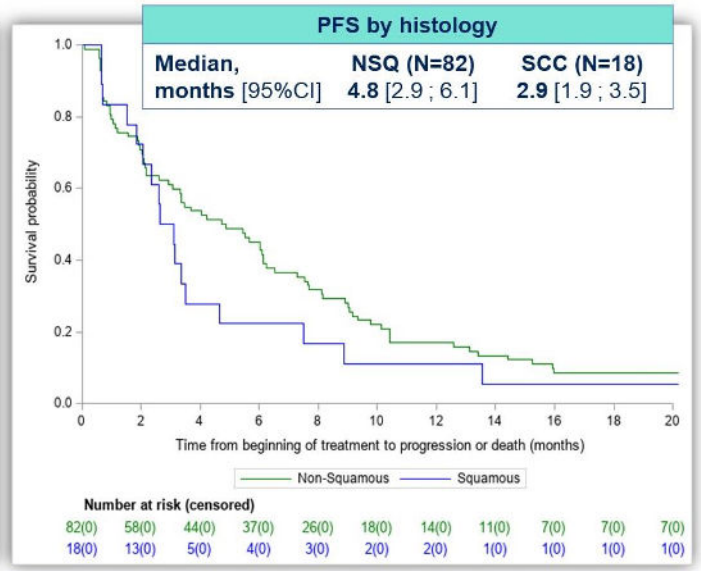


Anticorps conjugués (ADC's)

ICARUS : Datopotamab Deruxtecan

PFS: overall population and by histology



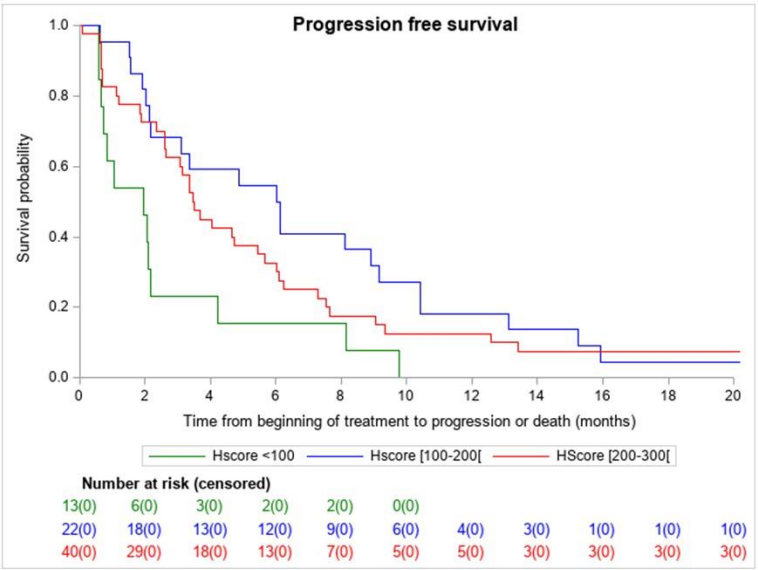


Median follow-up: 21.5 months [95%CI 19.4 ; 23.4]

Regardless of histology

Median PFS by EGFR, BRAFmut, months [95%CI]*	Present (N=12)	Absent (N=73)
	6.8 [0.8 ; 10.4]	3.3 [2.1 ; 5.7]

TROP2 expression and PFS



TROP2 (H-score)*	<100 (N = 13)	100-200 (N = 22)	≥200 (N = 40)
Median PFS, months [95% CI]	2.0 [0.7 ; 2.2]	6.1 [2.1 ; 9.2]	3.5 [2.6 ; 5.5]
HR** [95% CI]	ref	0.37 [0.18-0.75]	0.50 [0.26-0.94]

TROP2 (EPR20043) FLA IHC; H-Score: autocalculation of tumor cells staining intensity in the membrane compartment= (1[MEMBRANE 1+]) + (2*[MEMBRANE 2+]) + (3*[MEMBRANE 3+])

**p value = 0.02

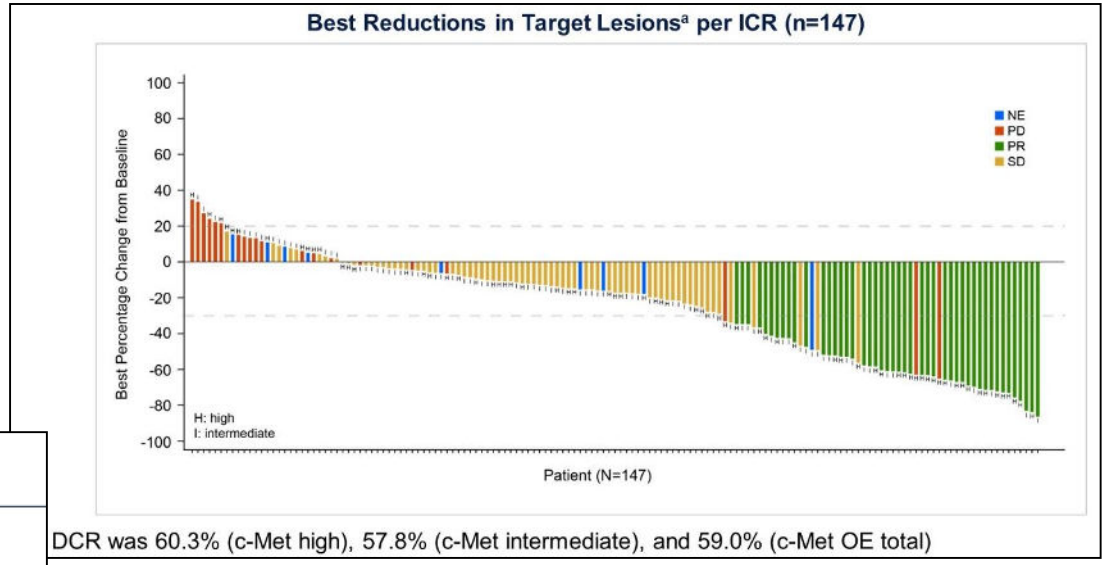
Patients with a wide range of **TROP2 expression** may benefit from Dato-DXd §

§ No statistically significant association with ORR

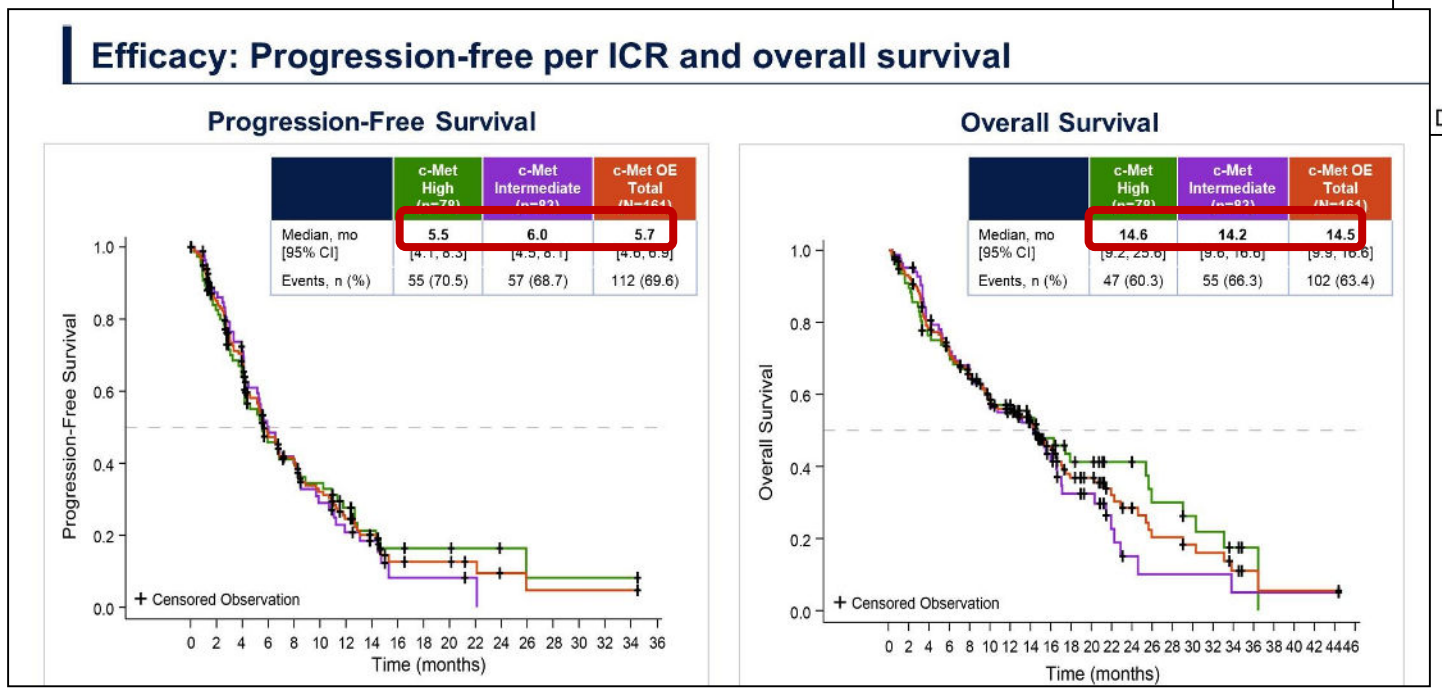
Planchard ; Abstr 8501

Anticorps conjugués (ADC's)

Telisotuzumab Vedotin



DCR was 60.3% (c-Met high), 57.8% (c-Met intermediate), and 59.0% (c-Met OE total)



- Autorisation d'accès précoce
- Carcinome non épidermoide MET+ en IHC

Camidge ; Abstr 103

Addictions oncogéniques

Mutations / Fusions

- EGFR
  - Classiques (del 19, L858R)
  - Non communes (G719x, S768I, L861Q)
  - Ins exon 20
- Kras (G12C)
- BRAF (V600)
- HER2 (exon20)
- MET (saut d'exon 14)

- ALK
- ROS1
- RET
- NTRK
- NRG1

Kras (G12C)

Adagrasib

KRYSTAL-12[a] study design

Key eligibility criteria
- Locally advanced or metastatic NSCLC with *KRAS*^{G12C} mutation[b]
- Prior treatment with platinum-based chemotherapy and anti-PD-(L)1 therapy[c]
- ECOG PS 0-1
- Stable brain metastases allowed

N = 453, R 2:1

- ADA 600 mg BID PO[d]
- DOCE 75 mg/m² Q3W IV

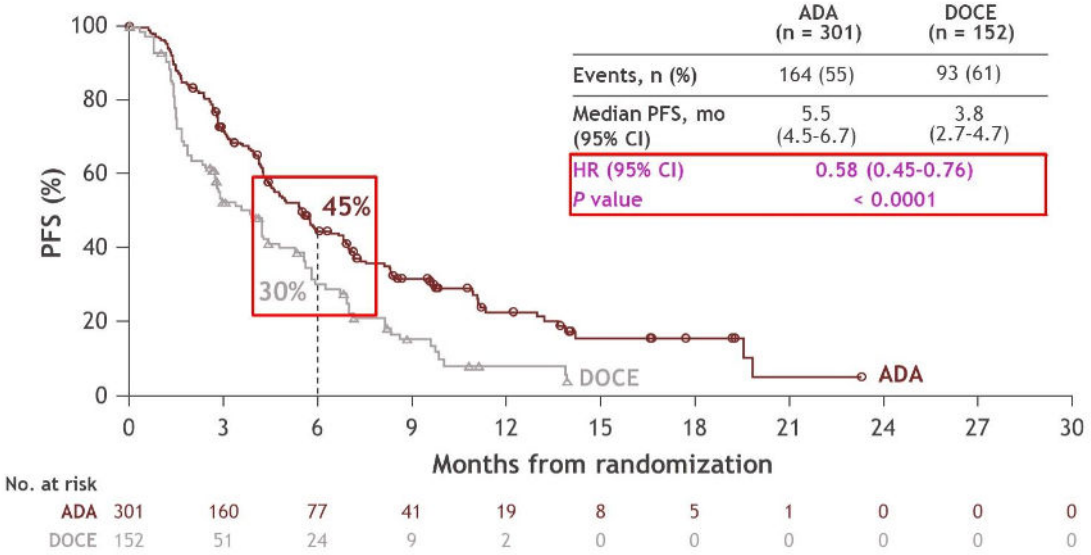
Crossover from DOCE to ADA was allowed in cases where disease progression per RECIST v1.1 was confirmed by real-time BICR[e]

Stratified by:
- Region (non-Asia-Pacific vs Asia-Pacific)
- Prior treatment (sequential vs concurrent chemotherapy and immunotherapy)

Primary endpoint
- PFS by BICR (RECIST v1.1)

Secondary endpoints
- ORR by BICR (RECIST v1.1)
- DOR
- OS
- Safety
- Patient-reported outcomes

Primary endpoint: PFS[a] per BICR



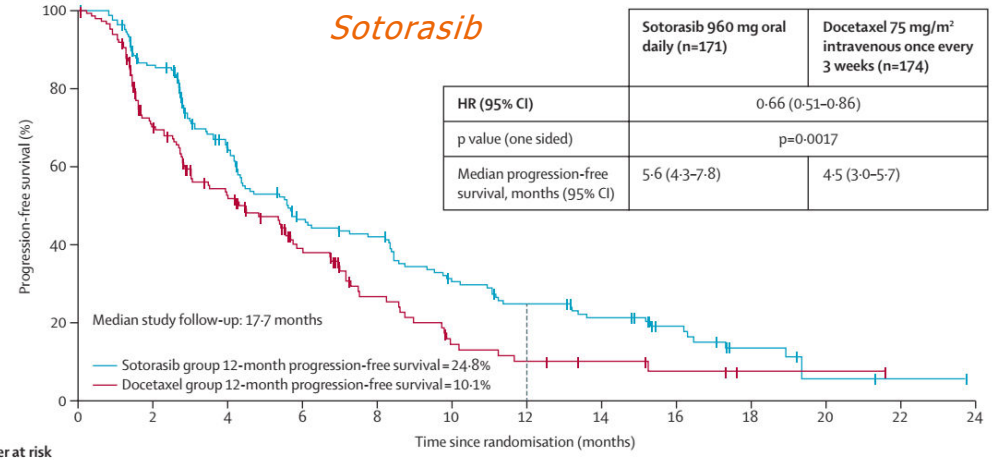
	ADA (n = 301)	DOCE (n = 152)
Events, n (%)	164 (55)	93 (61)
Median PFS, mo (95% CI)	5.5 (4.5-6.7)	3.8 (2.7-4.7)
HR (95% CI)	0.58 (0.45-0.76)	
P value	< 0.0001	

No. at risk

ADA	301	160	77	41	19	8	5	1	0	0	0
DOCE	152	51	24	9	2	0	0	0	0	0	0

Median follow-up: 7.2 months.
[a]Time from randomization to the date of disease progression per BICR or death due to any cause, whichever occurs first. For patients who started a subsequent anticancer therapy prior to disease progression or death, PFS was censored at the date of the last tumor assessment prior to the start of the new therapy.

Sotorasib



	Sotorasib 960 mg oral daily (n=171)	Docetaxel 75 mg/m² intravenous once every 3 weeks (n=174)
HR (95% CI)	0·66 (0·51–0·86)	
p value (one sided)	p=0·0017	
Median progression-free survival, months (95% CI)	5·6 (4·3–7·8)	4·5 (3·0–5·7)

Number at risk (number censored)

Sotorasib group	171 (0)	139 (9)	93 (14)	63 (4)	56 (1)	38 (3)	30 (1)	24 (2)	14 (8)	6 (4)	2 (1)	1 (1)	0 (1)
Docetaxel group	174 (0)	93 (39)	62 (9)	36 (12)	20 (6)	10 (1)	7 (0)	5 (2)	3 (1)	1 (2)	1 (0)	0 (1)	..

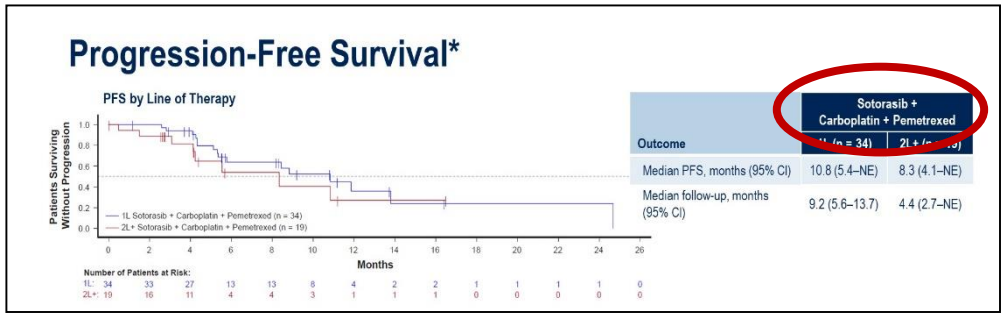
Tony Mok ; LBA8509

Johannes de Langen ; Lancet 2023 ; 401:733-746

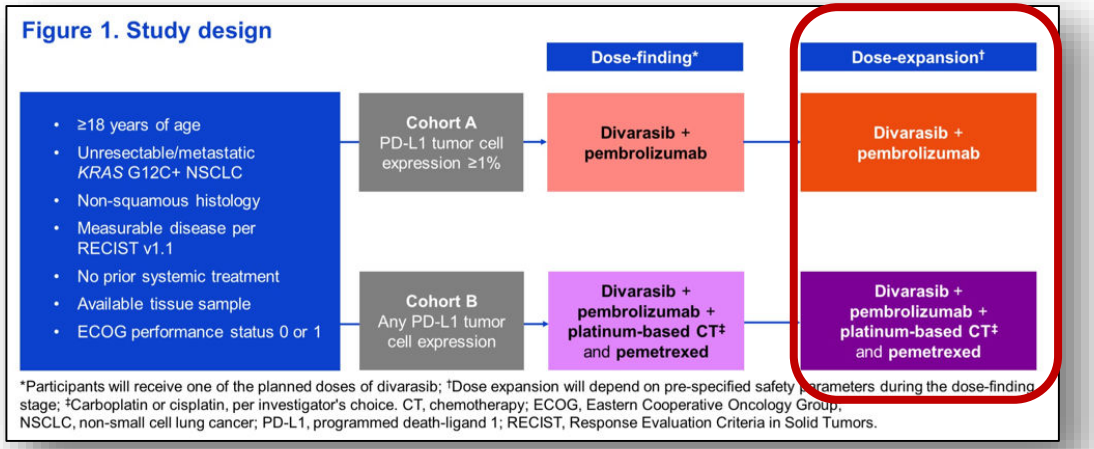
KRas (G12C)

Olomorasib, Divarasib

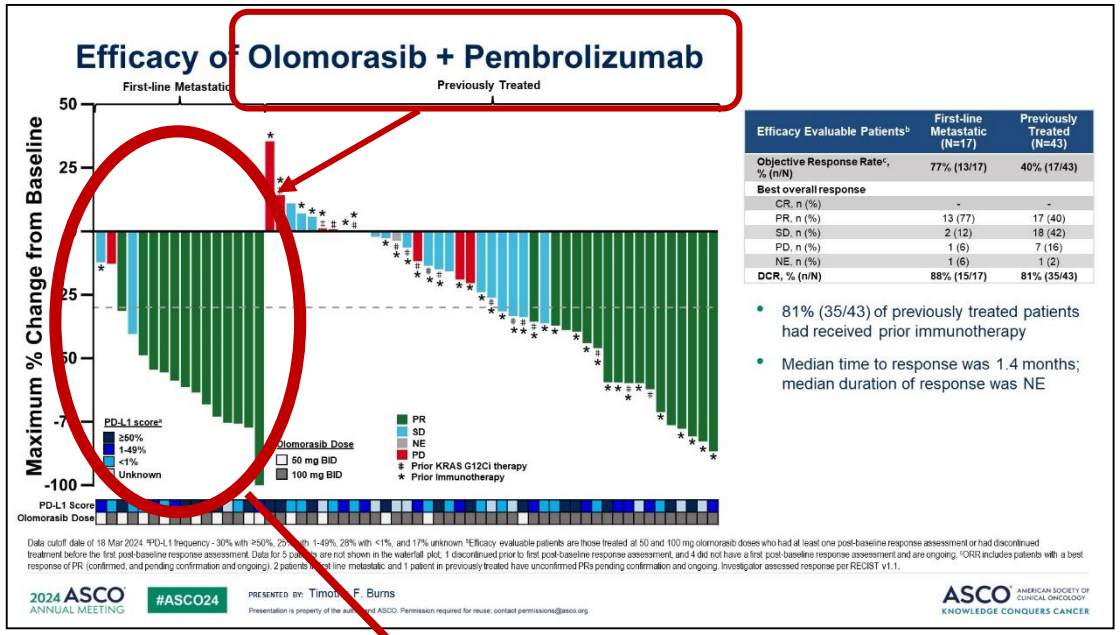
- Dès la 1ère ligne
- Associations avec ICI

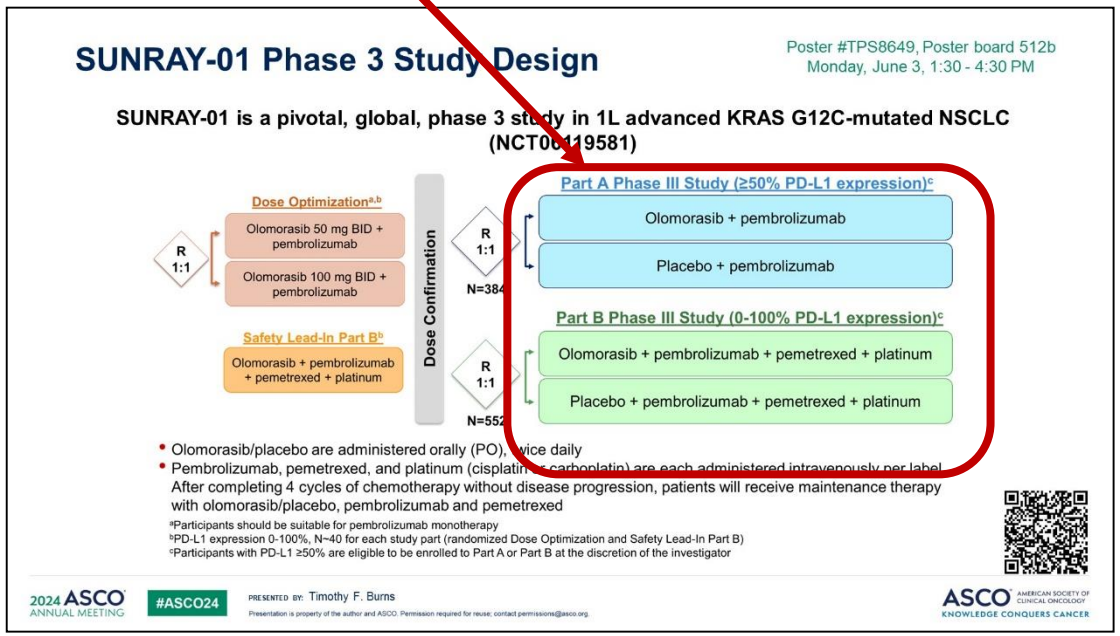


Li ; Abstr 8512



Skoulidis ; TPS8651

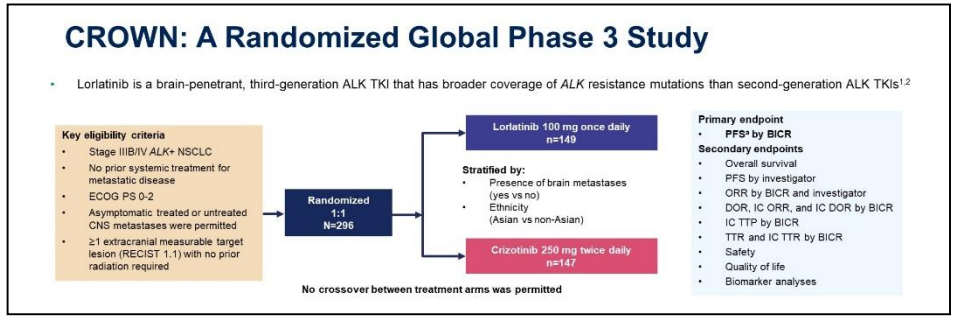




Suk Heist ; Abstr 3007

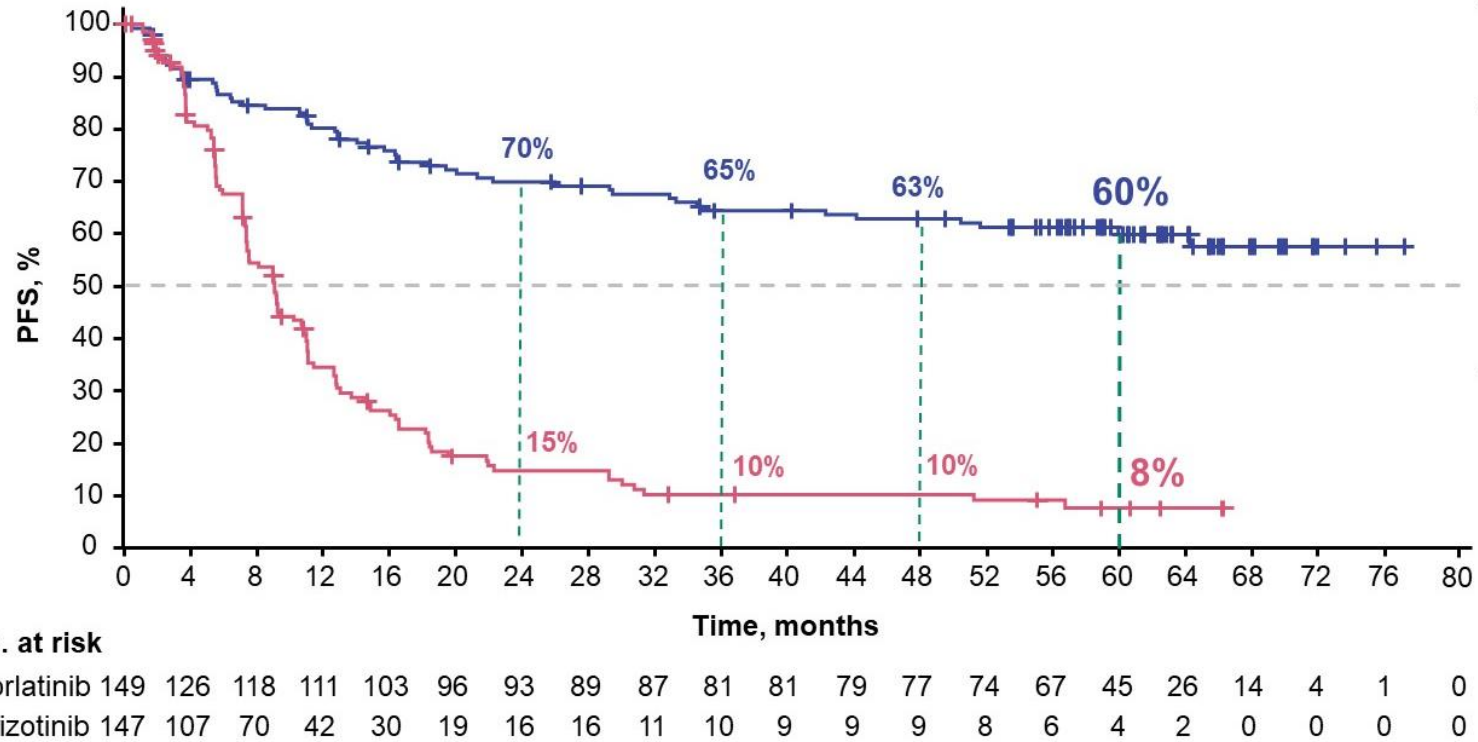
ALK

Lorlatinib



Solomon ; LBA8503

At 60.2 Months of Median Follow-Up, Median PFS by Investigator Was Still Not Reached With Lorlatinib



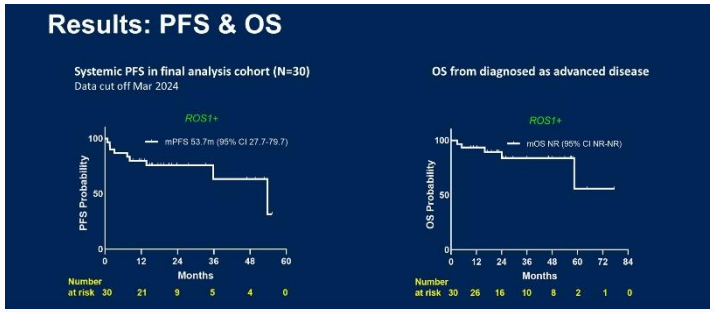
	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	55	115
PFS, median (95% CI), months	NR (64.3-NR)	9.1 (7.4-10.9)
HR (95% CI)	**0.19 (0.13-0.27)**	

At the time of this analysis, the required number of OS events for a protocol-specified second interim analysis **has not been reached**. OS follow up is ongoing

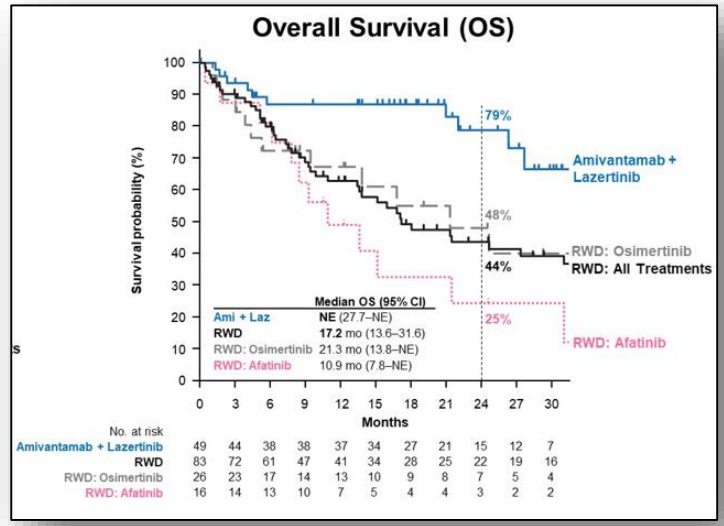
HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

Addictions oncogéniques

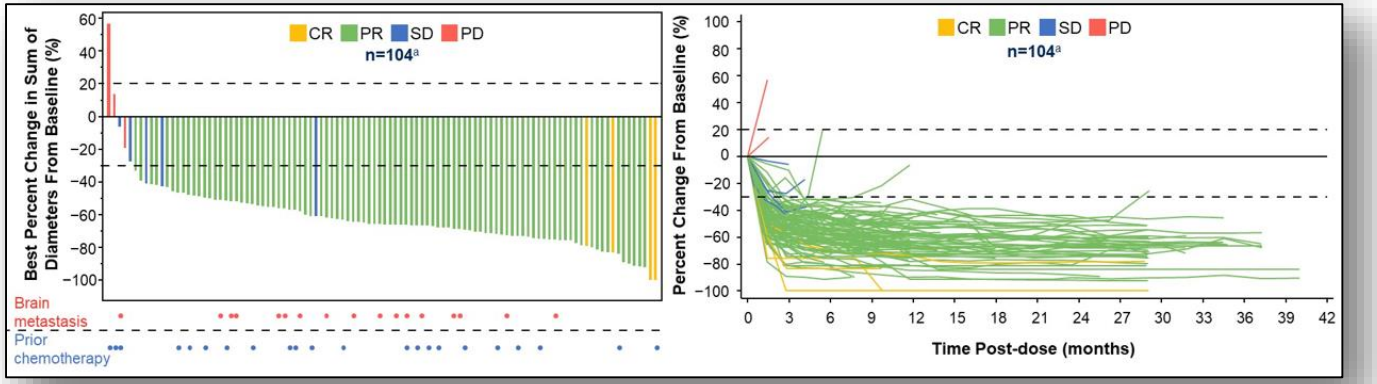
En vrac



Lorlatinib ROS1 (Ahn ; 8519)

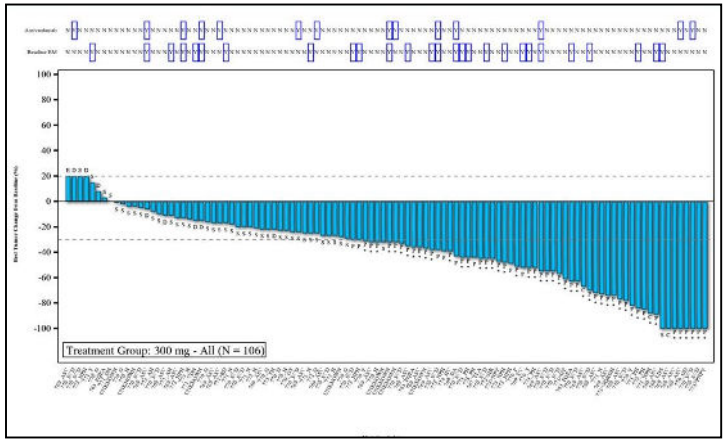


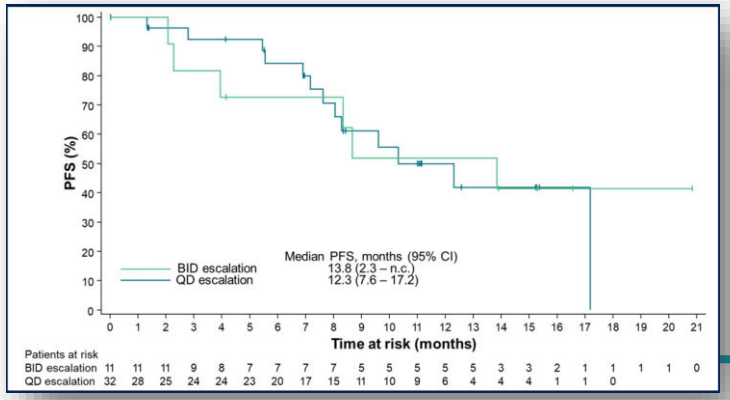
Amivantamab Lazertinib EGFR mutations non communes (Chul Cho ; 8516)



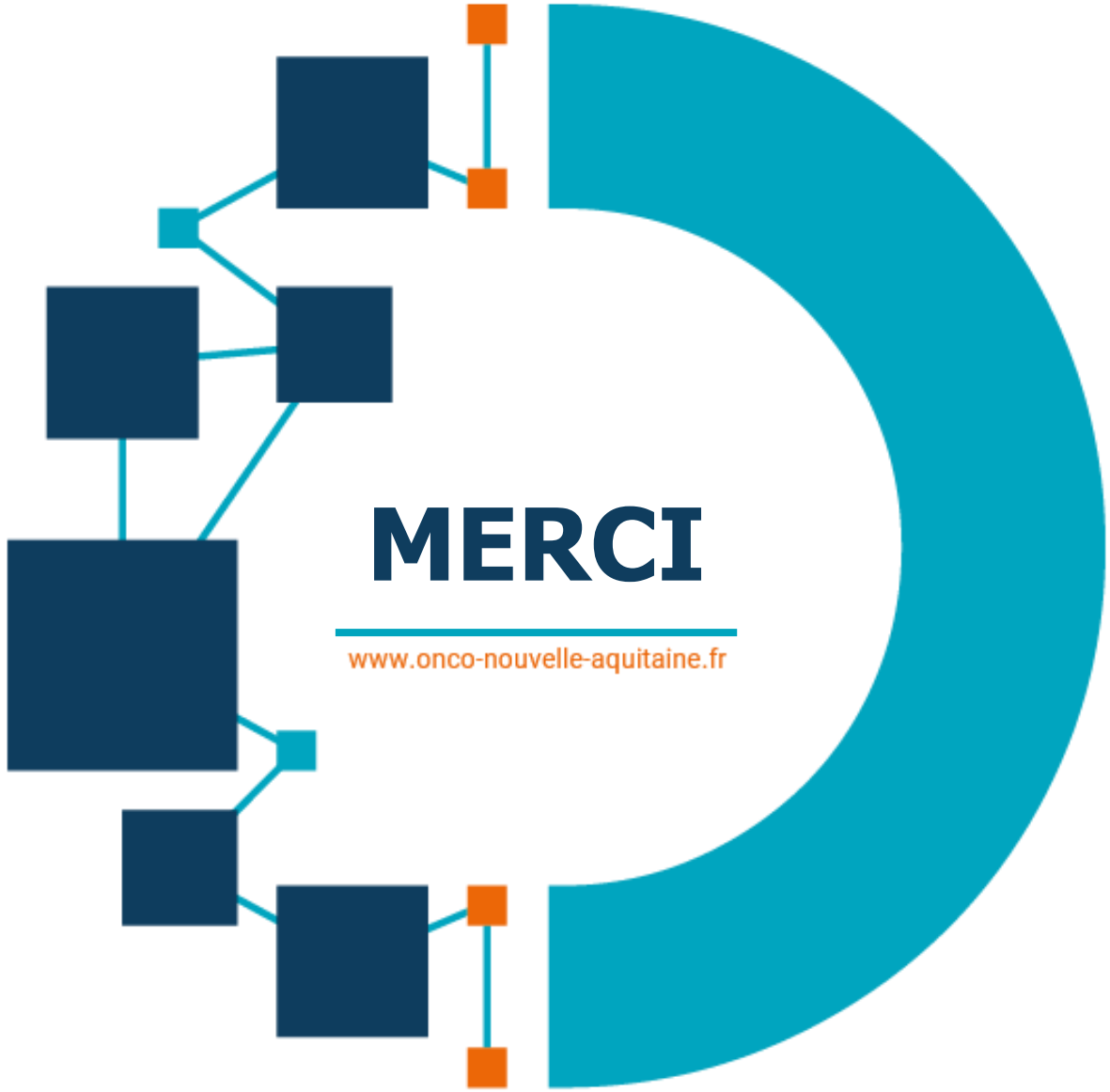
Taletrectinib ROS1 (Li ; 8520)

Sunvozertinib EGFRex20 (Yang ; 8513)





Zongertinib HER2 (et NRG1 ?) (Heymach ; 8514)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