Les immanquables de l'ESMO

5 Octobre 2021

CHU Bordeaux

Amaury Daste

ESMO en VRAC

Sélection
Phases 3
ou
Phases 2 significatives

Mélanome

1036O - Relatlimab (RELA) + nivolumab (NIVO) vs. NIVO

Study design

- **RELA**TIVITY-047 is a global, randomized, double-blind, phase 2/3 study

Key eligibility criteria
- Previously untreated metastatic or unresectable melanoma[a]
- ECOG PS 0-1

Stratification factors
- LAG-3[b]
- PD-L1[c]
- *BRAF*
- AJCC v8 M stage

N = 714

R 1:1

- RELA 160 mg + NIVO 480 mg FDC IV Q4W
- NIVO 480 mg IV Q4W

Primary endpoint
- PFS by BICR[d]

Secondary endpoints
- OS
- ORR by BICR[d]

Exploratory endpoints included:
- TFI
- PFS2

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; CTLA-4, cytotoxic T lymphocyte antigen-4; ECOG PS, Eastern Cooperative Oncology Group performance status; FDC, fixed-dose combination; IHC, immunohistochemistry; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS2, progression-free survival 2; Q4W, every 4 weeks; R, randomization; RECIST, Response Evaluation Criteria In Solid Tumors; TFI, treatment-free interval.
[a]Prior adjuvant/neoadjuvant treatment permitted (anti-PD-1 or anti-CTLA-4 permitted if ≥ 6 months between the last dose and recurrence; interferon therapy permitted if the last dose was ≥ 6 weeks before randomization); [b]LAG-3 expression on immune cells was determined using an analytically validated IHC assay (LabCorp); [c]PD-L1 expression on tumor cells was determined using the validated Agilent/Dako PD-L1 IHC 28-8 pharmDx test; [d]First tumor assessment (RECIST v1.1) performed 12 weeks after randomization, every 8 weeks up to 52 weeks, and then every 12 weeks. Database lock date: March 9, 2021.
ClinicalTrials.gov: NCT03470922; Lipson EJ, et al. American Society of Clinical Oncology Congress; June 4-8, 2021. Abstract number 9503.

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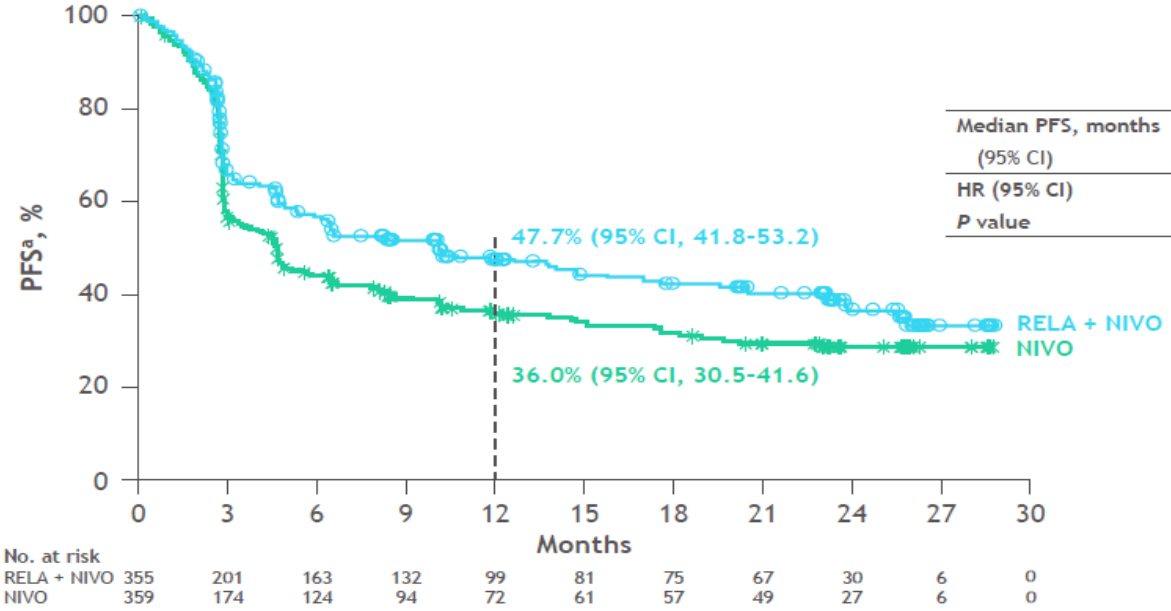
Mélanome

1036O - Relatlimab (RELA) + nivolumab (NIVO) vs. NIVO

RELATIVITY-047 demonstrated superior PFS benefit for RELA + NIVO versus NIVO



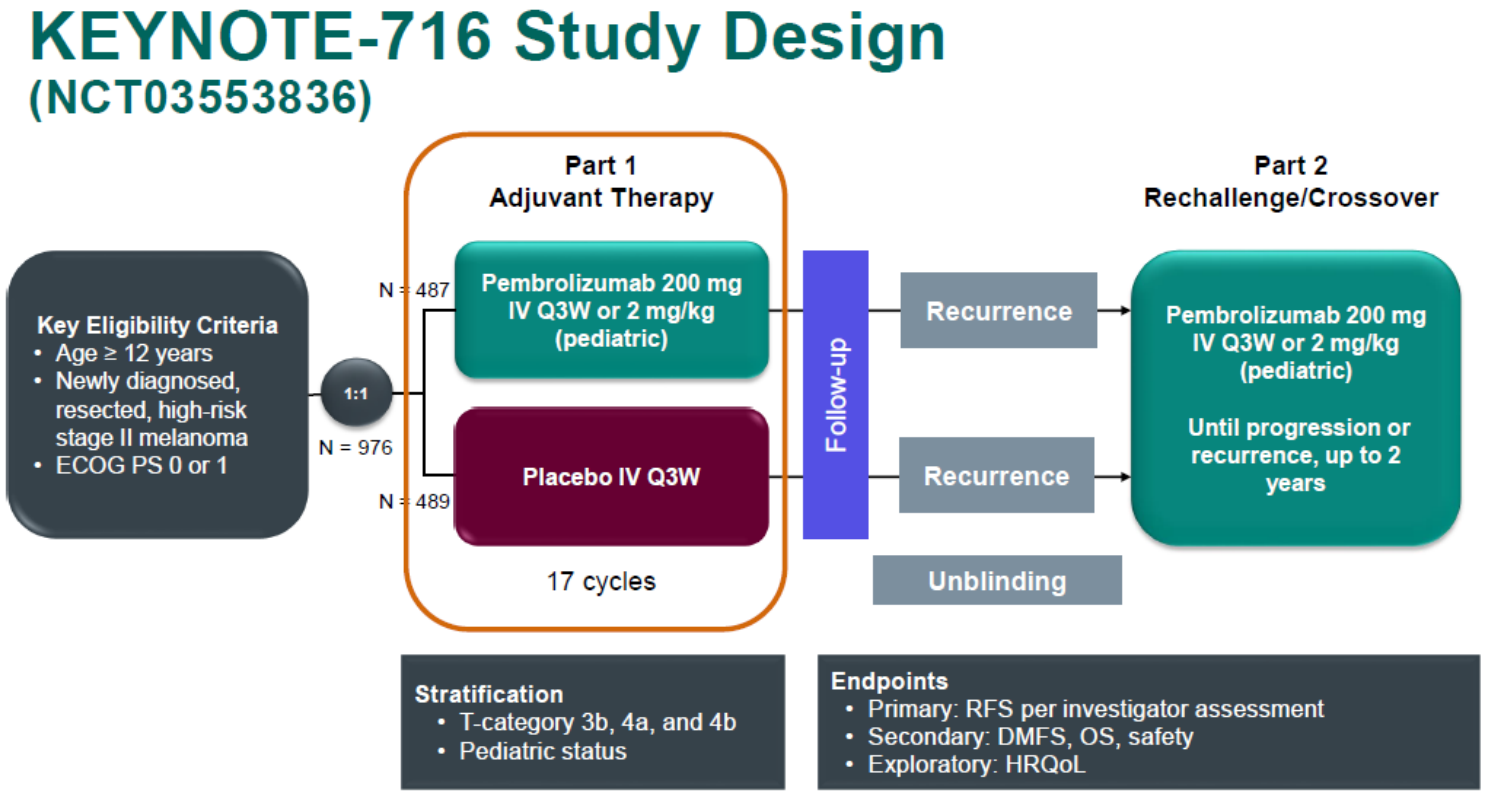
	RELA + NIVO (n = 355)	NIVO (n = 359)
Median PFS, months	10.12	4.63
(95% CI)	(6.37-15.74)	(3.38-5.62)
HR (95% CI)	0.75 (0.62-0.92)	
P value	0.0055	

CI, confidence interval; HR, hazard ratio.
[a]PFS was assessed by blinded independent committee review. Median follow-up was 13.2 months. All randomized patients. Statistical model for HR and *P* value: stratified Cox proportional hazard model and stratified log-rank test. Stratified by LAG-3 (≥ 1% vs < 1%), *BRAF* (mutation positive vs mutation wild-type), AJCC M stage (M0/M1any[0] vs M1any[1]). PD-L1 was removed from stratification because it led to subgroups with < 10 patients.
Lipson EJ, et al. American Society of Clinical Oncology Congress; June 4-8, 2021. Abstract number 9503.

- Bras de comparaison nivo/ipi (mPFS: 11,5 mois)
- G3-4 18,9%; arrêt 8,5%

Mélanome

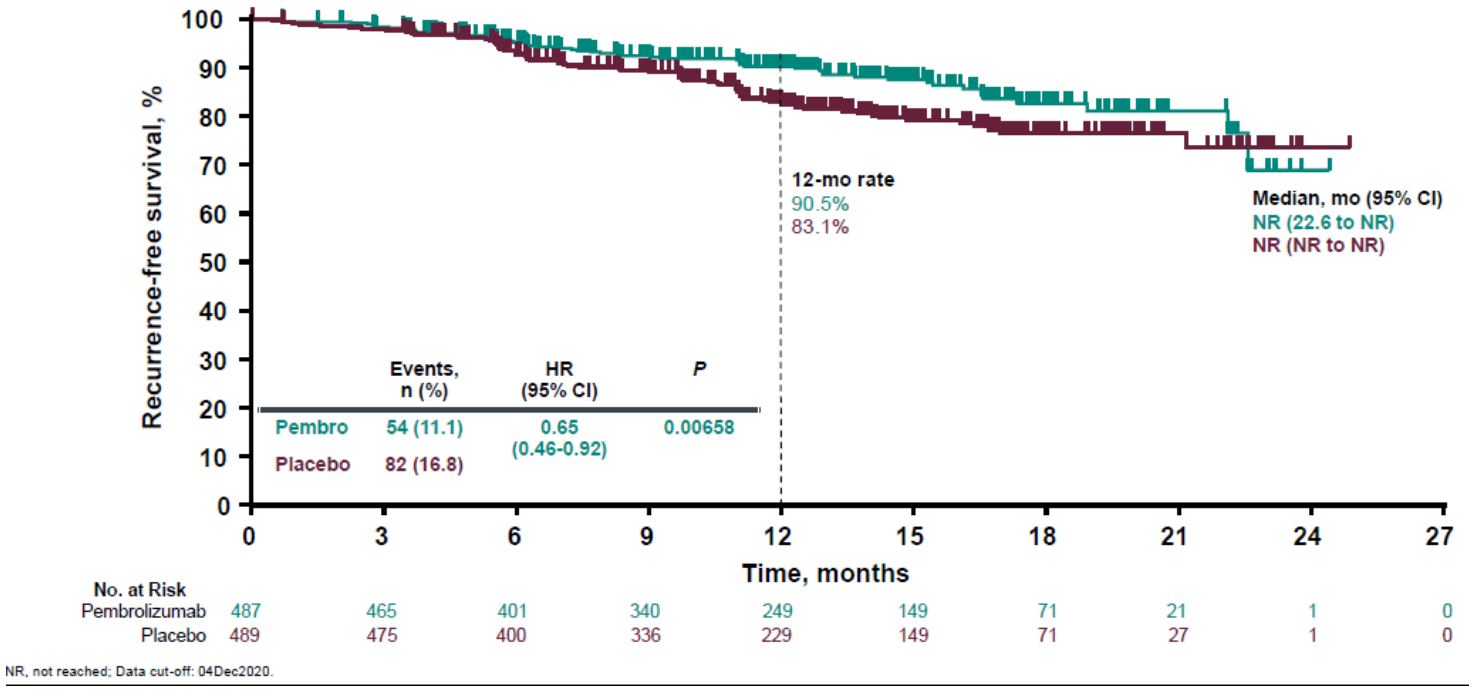
LBA3_PR - Pembrolizumab versus placebo after complete resection



Mélanome

LBA3_PR - Pembrolizumab versus placebo after complete resection

Recurrence-Free Survival (Primary Endpoint)



NR, not reached; Data cut-off: 04Dec2020.

- Moins d'effets dans sous groupe T4b
- Qualité de vie préservée

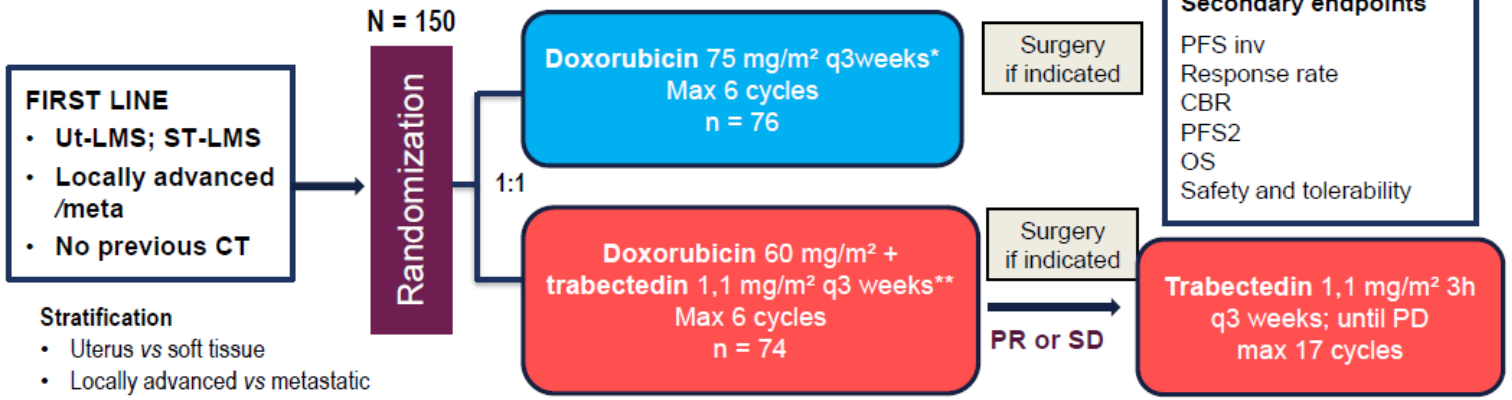
Event, n (%)	Pembrolizumab N = 487	Placebo N = 489
Patients without an event	433 (88.9%)	407 (83.2%)
Patients with an event[a]	54 (11.1%)	82 (16.8%)
Skin and/or LN regional recurrence	31 (6.4%)	41 (8.4%)
Distant recurrence	23 (4.7%)	38 (7.8%)

Sarcome

LBA59 - LMS-04 study: A randomised, multicenter, phase III study comparing doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin

Study design

LMS 04: Ph-III first-line therapy for locally advanced/metastatic LMS



* + Lenograstim 150 µg/m²/day s.c. d3-9; **+ Pegfilgrastim 6 mg s.c. day 2.

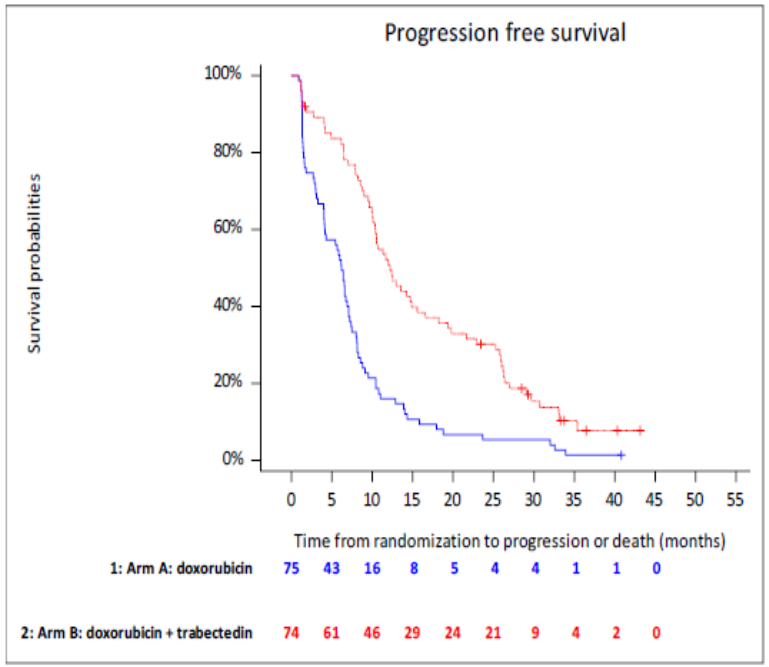
P. Pautier

PFS: progression-free-survival; RX: radiological; CBR: clinical benefice rate; PFS inv: investigator-assessed PFS.

Sarcome

LBA59 - LMS-04 study: A randomised, multicenter, phase III study comparing doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin

PFS by BICR, ITT population



BICR, blinded independent central review; ITT: intent to treat; CI, confidence interval; HR, hazard ratio; PFS: progression-free survival; **Median follow-up was 37 months**

	Doxo (N = 76)	Doxo + Trab (N = 74)
Events, n (%)	74 (97%)	65 (88%)
Median PFS, months	**6.2**	**12.2**
	HR 0.41	
	95% CI 0.29-0.58; *P*<0.0001	

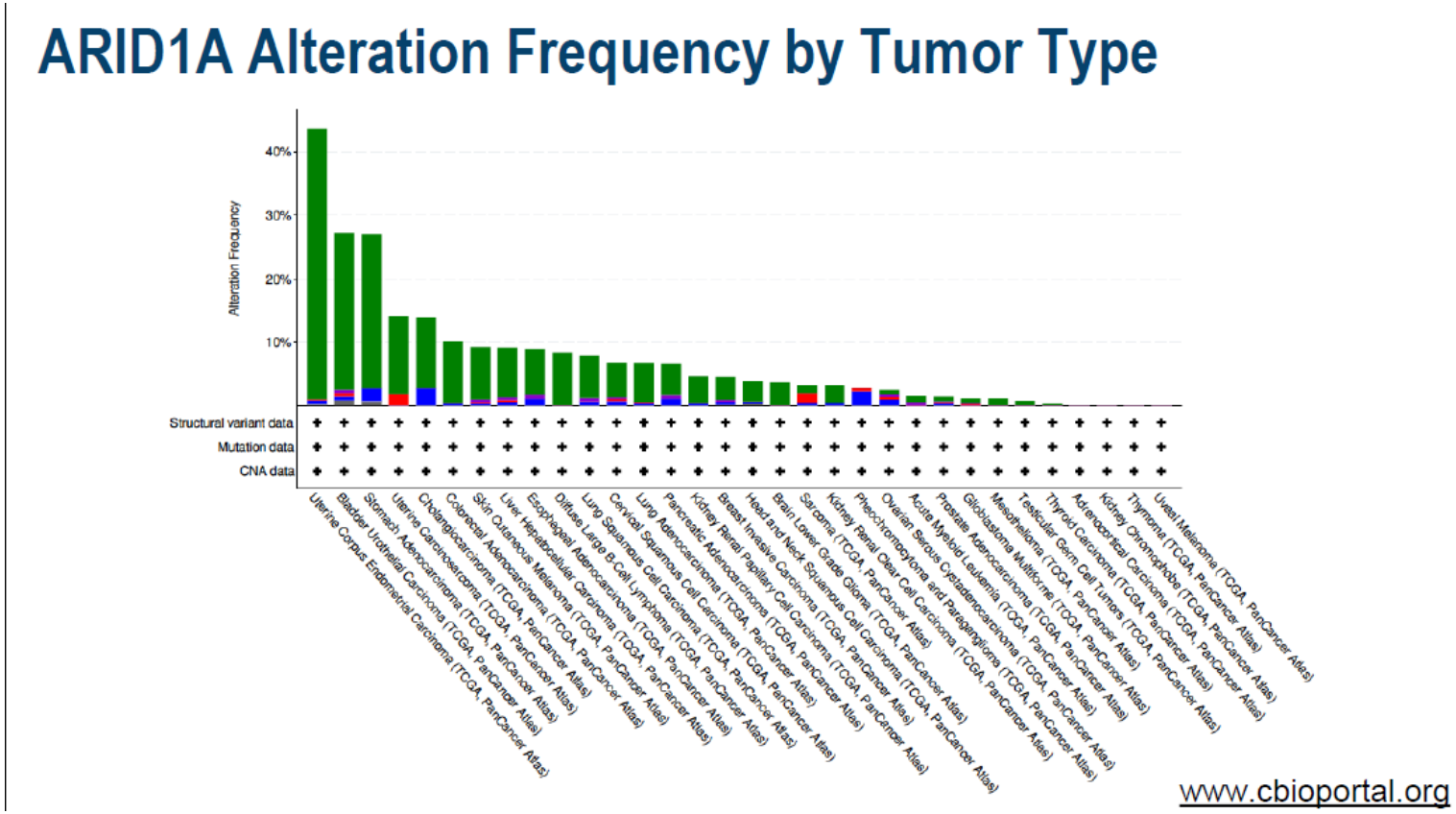
	Doxo (N = 76)	Doxo + Trab (N = 74)
Deaths, n (%)	50 (66%)	42 (57%)
Median OS, months	**24.1**	**30.5**
	HR 0.73	
	95% CI: 0.49-1.12	

Median follow-up : 37 months

	Doxo N = 76	Doxo + Trab N = 74
Response		
➢ CR	0	4 (5%)
➢ PR	10 (13%)	24 (32%)
➢ SD	50 (66%)	40 (54%)
Response Rate before surgery n (%)	**10 (13%)**	**28 (38%)**
Ut-LMS (n = 67)	5 (15%)	12 (36%)
ST-LMS (n = 83)	5 (12%)	16 (39%)

Drugs development

512O - Interim results from a phase II study of the ATR inhibitor ceralasertib in ARID1A-deficient and ARID1A-intact advanced solid tumor malignancies



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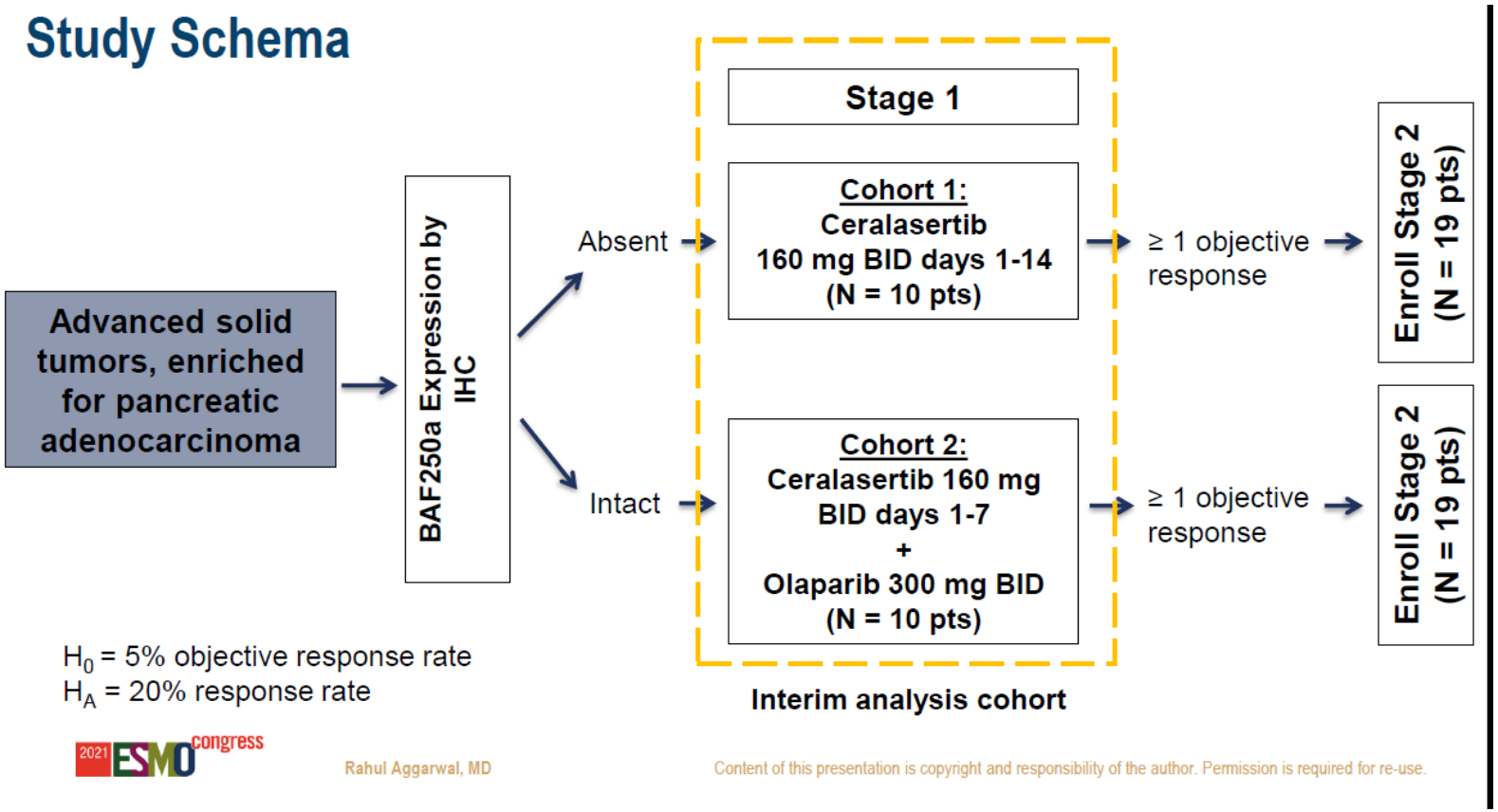
Drugs development

512O - Interim results from a phase II study of the ATR inhibitor ceralasertib in ARID1A-deficient and ARID1A-intact advanced solid tumor malignancies



Drugs development

512O - Interim results from a phase II study of the ATR inhibitor ceralasertib in ARID1A-deficient and ARID1A-intact advanced solid tumor malignancies

Best Overall Response

	Cohort 1: ARID1A-deficient N = 10 Ceralasertib monotherapy	Cohort 2: ARID1A-intact N = 10 Ceralasertib + olaparib
Complete response	2 (20)*	0
Partial Response	0	0
Stable Disease (%)	3 (30)	3 (30)
Progressive Disease (%)	5 (50)	7 (70)
Confirmed objective response (%)	2 (20)	0
Clinical benefit rate (ORR + SD > 6 months)	3 (30)	1 (10)

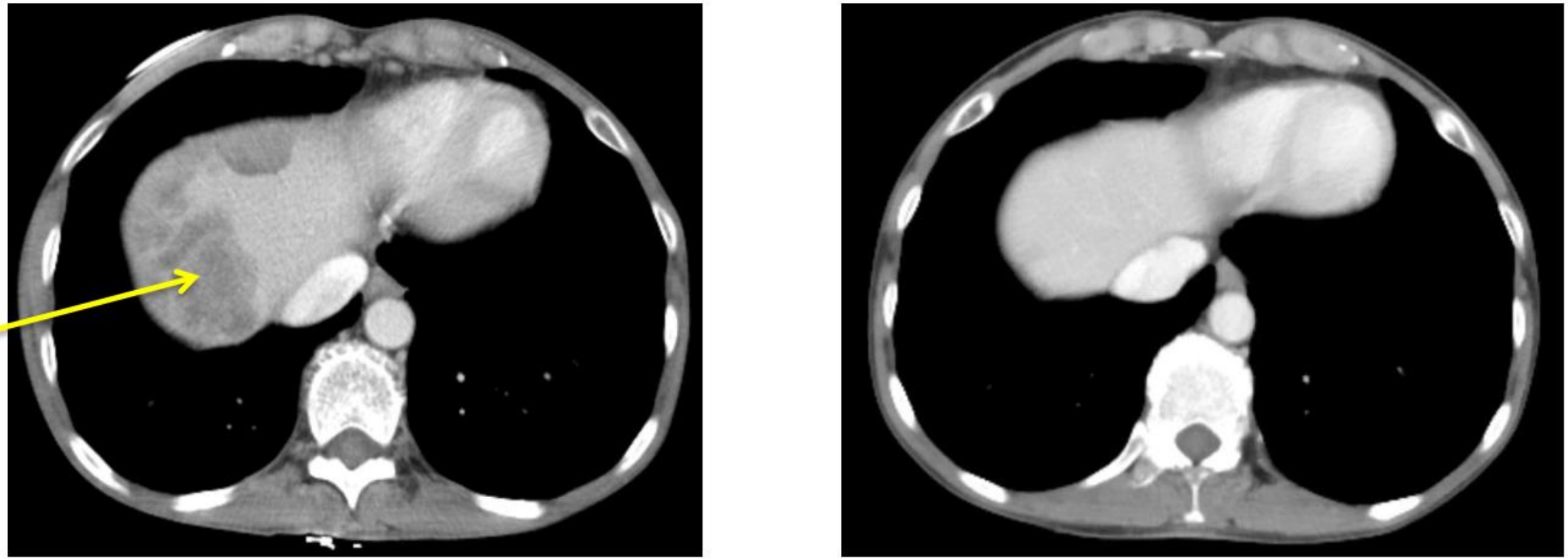
* Duration of response of 21.3+ and 16.3+ months, respectively

Drugs development

512O - Interim results from a phase II study of the ATR inhibitor ceralasertib in ARID1A-deficient and ARID1A-intact advanced solid tumor malignancies

Baseline

Post 21 months of treatment



Subcapsular liver metastases

Drugs development

512O - Interim results from a phase II study of the ATR inhibitor ceralasertib in ARID1A-deficient and ARID1A-intact advanced solid tumor malignancies

Cohort 1: Ceralasertib Monotherapy

Treatment-Related Adverse Events	Grade 1-2 (%)	Grade ≥ 3 (%)
Nausea	6 (60)	0
Vomiting	4 (40)	0
Thrombocytopenia	1 (10)	1 (10)
Anemia	4 (40)	0
Neutropenia	0	2 (20)
Fatigue	3 (30)	0

- 4 patients (40%) required one dose level reduction
- No patients discontinued for adverse events

Neuro-endocrine

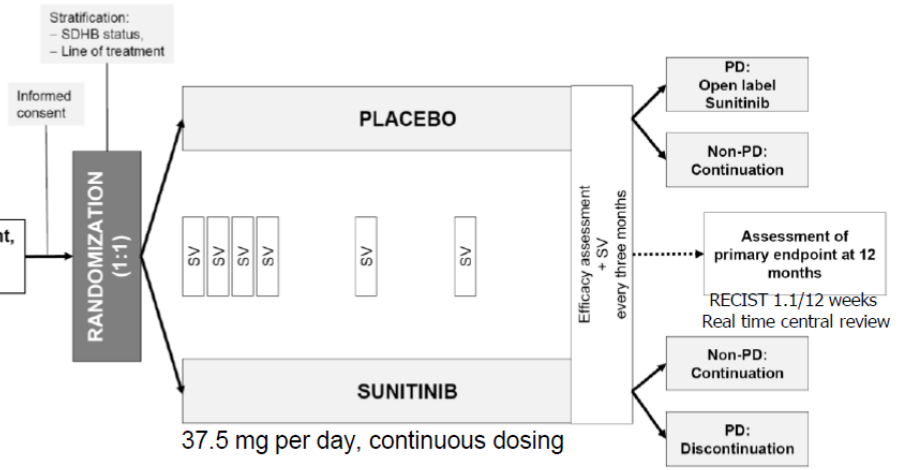
567O_PR - First International Randomized Study in Malignant Progressive Pheochromocytoma and Paragangliomas (FIRSTMAPPP)

FIRSTMAPPP design : double-blind academic randomized phase II trial in MPPGL

15 participating centers across 4 european countries

Main inclusion criteria
- Metastatic disease
- Pre-treated or not
- Inherited or not
- Evaluable, RECIST 1.1 criteria
- Progressing disease within 18 months according to RECIST

Main exclusion criteria
- Hypertension that cannot be controlled
- Abnormal cardiac function
- Prior tyrosine kinase inhibitors or anti-VEGF angiogenic inhibitors



2021 ESMO congress

Baudin E et al. 2021

Date of first randomized patients : 22 Dec 2011 – Date of DB lock : 3rd May 2021

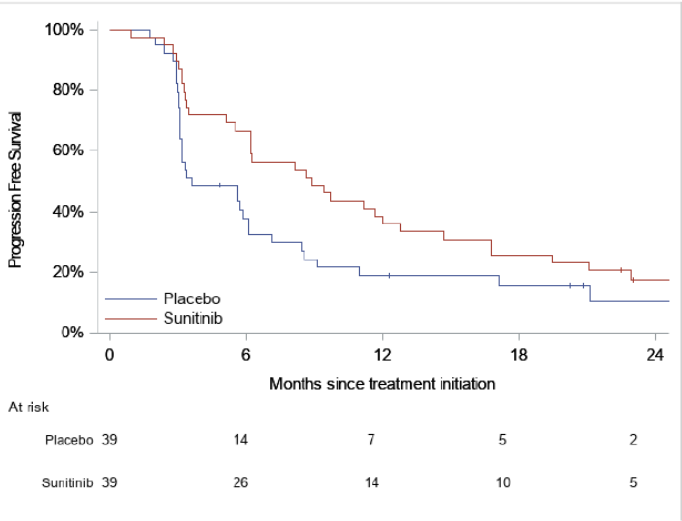
Neuro-endocrine

567O_PR - First International Randomized Study in Malignant Progressive Pheochromocytoma and Paragangliomas (FIRSTMAPPP)

FIRSTMAPPP : MEDIAN PFS

median PFS in both arms

Median PFS is
- 8.9 months in Sunitinib arm (95% CI: [5.5; 12.7])
- 3.6 months in Placebo arm (95% CI: [3.1; 6.1]).



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Neuro-endocrine

1096O - Lanreotide autogel/depot (LAN) in patients with advanced bronchopulmonary (BP) neuroendocrine tumors (NETs)

SPINET: study design and methods

Design

Phase 3, DB, randomized, placebo-controlled study of LAN (120 mg/28 days), with optional OL LAN treatment phase (EudraCT 2015-004992-62; NCT02683941)

Enrollment stopped due to slow accrual (European and US guidelines updated to include SSAs as 1L option for BP-NETs)

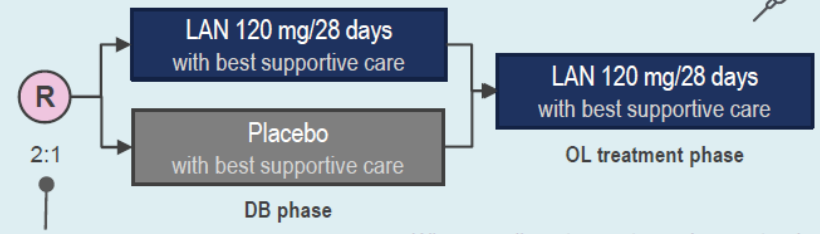
Key inclusion criteria

- Aged ≥ 18 years
- Metastatic and/or unresectable, well-differentiated BP-NETs (TC or AC)
- Mitotic index < 2 mitoses/2 mm^3 (TC) or ≤ 10 mitoses/2 mm^3 and/or foci of necrosis (AC)
- Positive SSTR imaging
- ECOG PS score of 0 or 1

Key exclusion criteria

- Previous SSA treatment[a]
- Prior treatment with ≥ 2 lines of chemotherapy[b] for BP-NETs

Treatment



Stratified by tumor type (TC/AC) and previous chemotherapy (yes/no)

When enrollment was stopped prematurely, patients whose disease had not progressed (central assessment) during DB treatment were switched to open-label LAN[c]

Endpoints

- **Adapted primary endpoint**: PFS (centrally assessed, RECIST 1.1) during DB and OL phases in patients randomized to LAN
  Adapted after enrollment stopped
- **Secondary endpoints** included:
  - PFS, ORR, and TTF in LAN and placebo groups during DB phase
  - Safety

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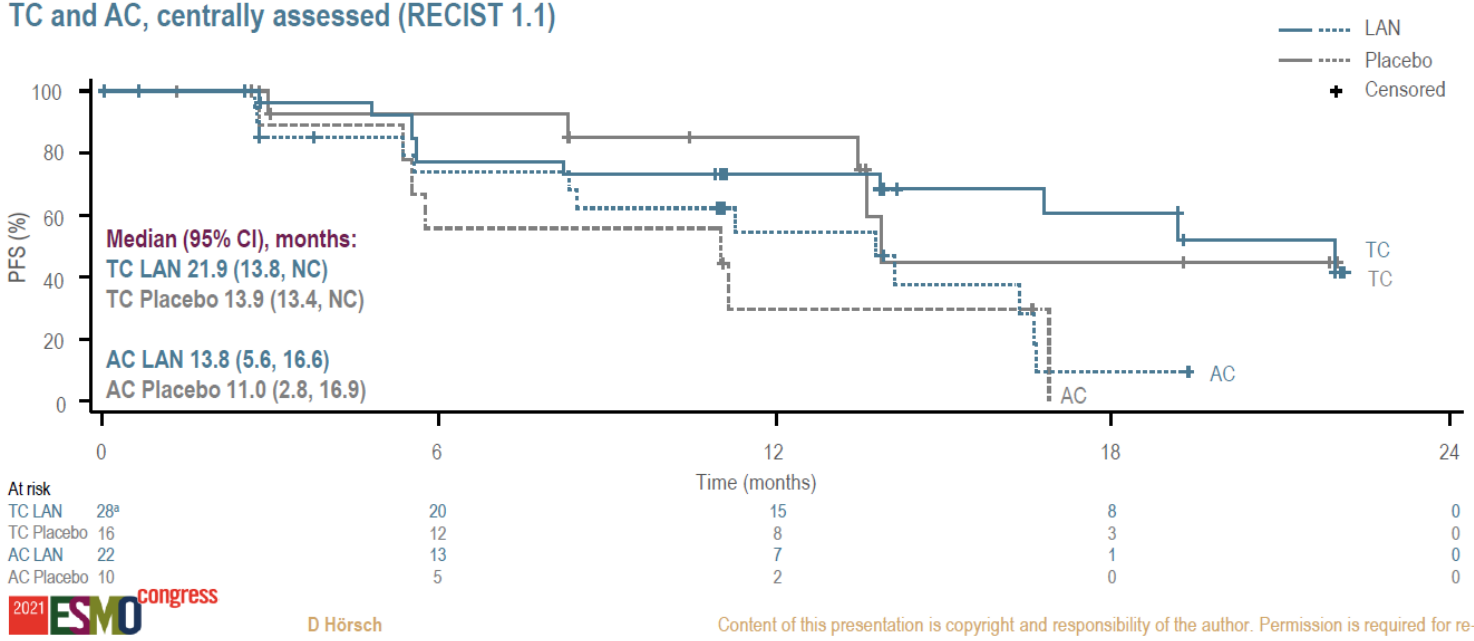
D Hörsch

Neuro-endocrine

1096O - Lanreotide autogel/depot (LAN) in patients with advanced bronchopulmonary (BP) neuroendocrine tumors (NETs)

SPINET: progression-free survival during DB phase by tumor type (WHO classification)

During DB treatment with LAN or placebo (ITT)
TC and AC, centrally assessed (RECIST 1.1)



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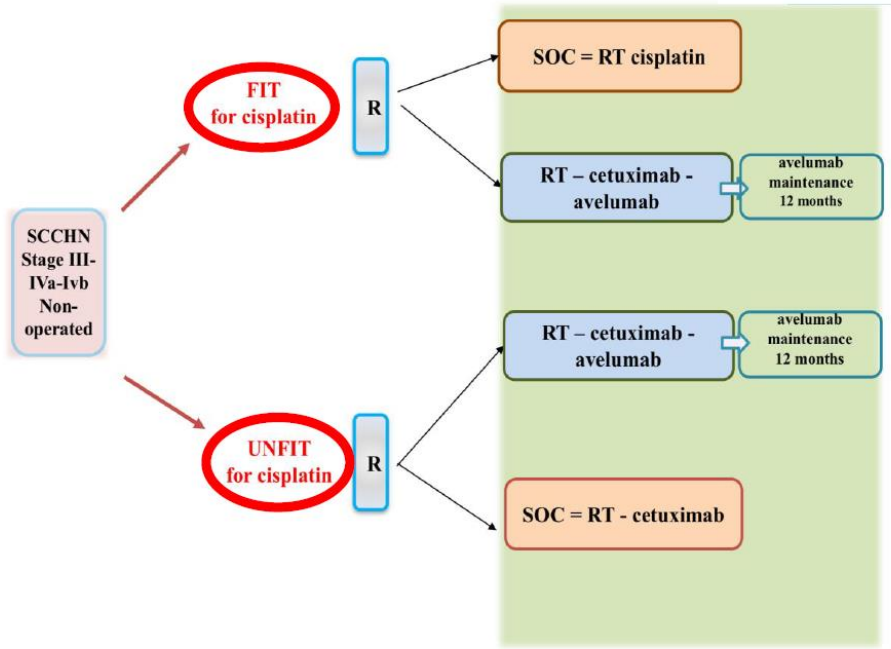
ORL

LBA35 - Avelumab-cetuximab-radiotherapy versus standards of care in patients with locally advanced squamous cell carcinoma of head and neck (LA-SCCHN)

Study design (II) & run in safety phase



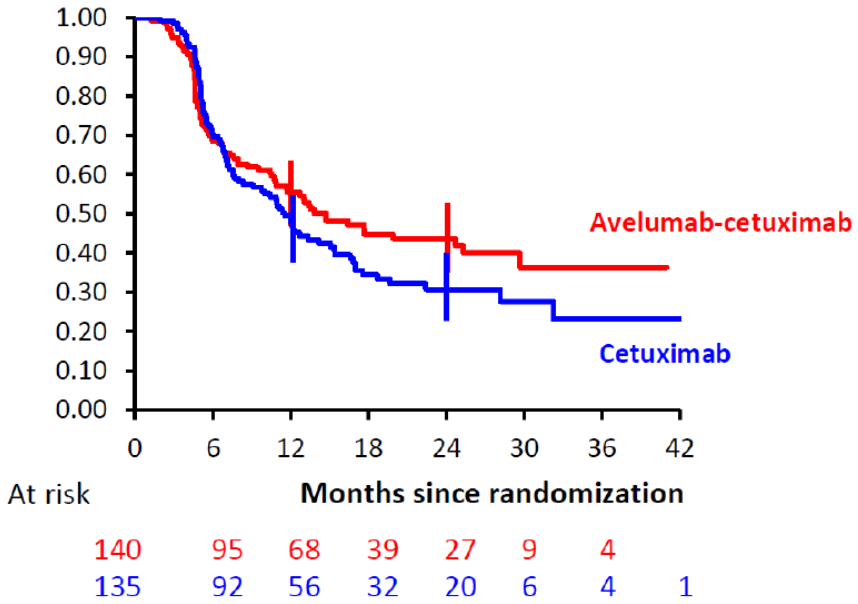
ORL

LBA35 - Avelumab-cetuximab-radiotherapy versus standards of care in patients with locally advanced squamous cell carcinoma of head and neck (LA-SCCHN)

Unfit Cohort : Primary endpoint

Kaplan Meier estimate of progression free survival (PFS)

Median follow-up = 21.3 months (IQR 14.6-28.3)(similar in both arms)



PFS at 2 years

44% (95%CI 35%-53%)
in Avelumab-Cetuximab
vs
31% (95%CI 23%-40%)
in Cetuximab

Adjusted* HR 0.84 for PFS
(95% CI 0.62-1.15)
one-sided p-value=0.14

- Efficacité non statistiquement significative
- Meilleur contrôle loco-régional
- Diminution des méta pour A/C
- Plus de décès dans les premiers mois bras A/C

ORL

LBA35 - Avelumab-cetuximab-radiotherapy versus standards of care in patients with locally advanced squamous cell carcinoma of head and neck (LA-SCCHN)

Cohort fit : summary

430 patients randomized

The number of PFS events was not reached, at the time of analysis

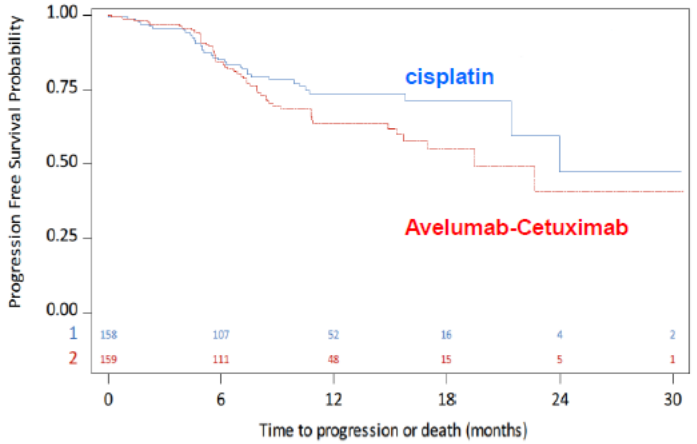
The planned interim analysis for futility based on 89 events in 317 patients showed a 1-year PFS rate of :

73% (95%CI 65%-81%) in SOC-cisplatin-RT

vs

64% (95%CI 54%-72%) in Avelumab-Cetuximab-RT

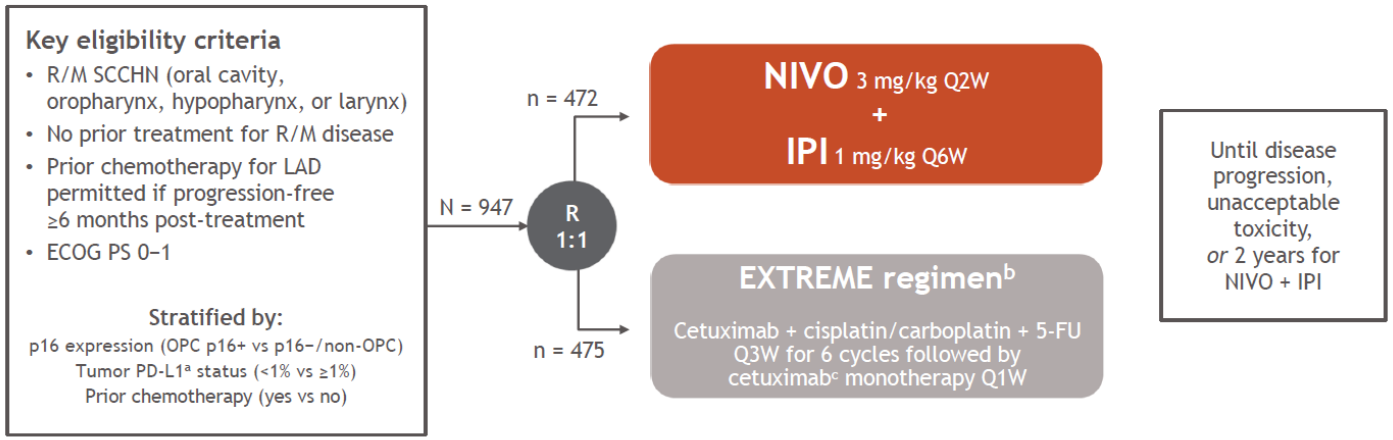
HR 1.27 (95%CI 0.83-1.93), crossing the futility boundary



ORL

LBA36 - Nivolumab (N) + ipilimumab (I) vs EXTREME as first-line (1L) treatment (tx) for recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN)

CheckMate 651 study design



Primary endpoints (independently tested)
- OS in all randomized
- OS in PD-L1 CPS[a] ≥20

Secondary endpoints
- OS in PD-L1 CPS ≥1[d]
- PFS by BICR (all randomized, PD-L1 CPS ≥20)
- ORR/DOR by BICR (all randomized, PD-L1 CPS ≥20)

Exploratory endpoints
- PFS and ORR/DOR in PD-L1 CPS ≥1
- Patient-reported outcomes
- Safety

NCT02741570. Database lock: June 21, 2021; minimum / median follow-up: 27.3 months / 39.1 months.
[a]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [b]Initial cetuximab dose of 400 mg/m² once only, then cetuximab 250 mg/m² Q1W plus cisplatin 100 mg/m² or carboplatin AUC 5 on day 1, plus fluorouracil 1000 mg/m²/d for 4 days for 6 cycles (Q3W); [c]Cetuximab 250 mg/m² Q1W; Q2W maintenance was allowed per local prescribing information; [d]Part of statistical testing hierarchy.
BICR, blinded independent central review; CPS, combined positive score; DOR, duration of response; LAD, locally advanced disease; OPC, oropharyngeal cancer; ORR, objective response rate.

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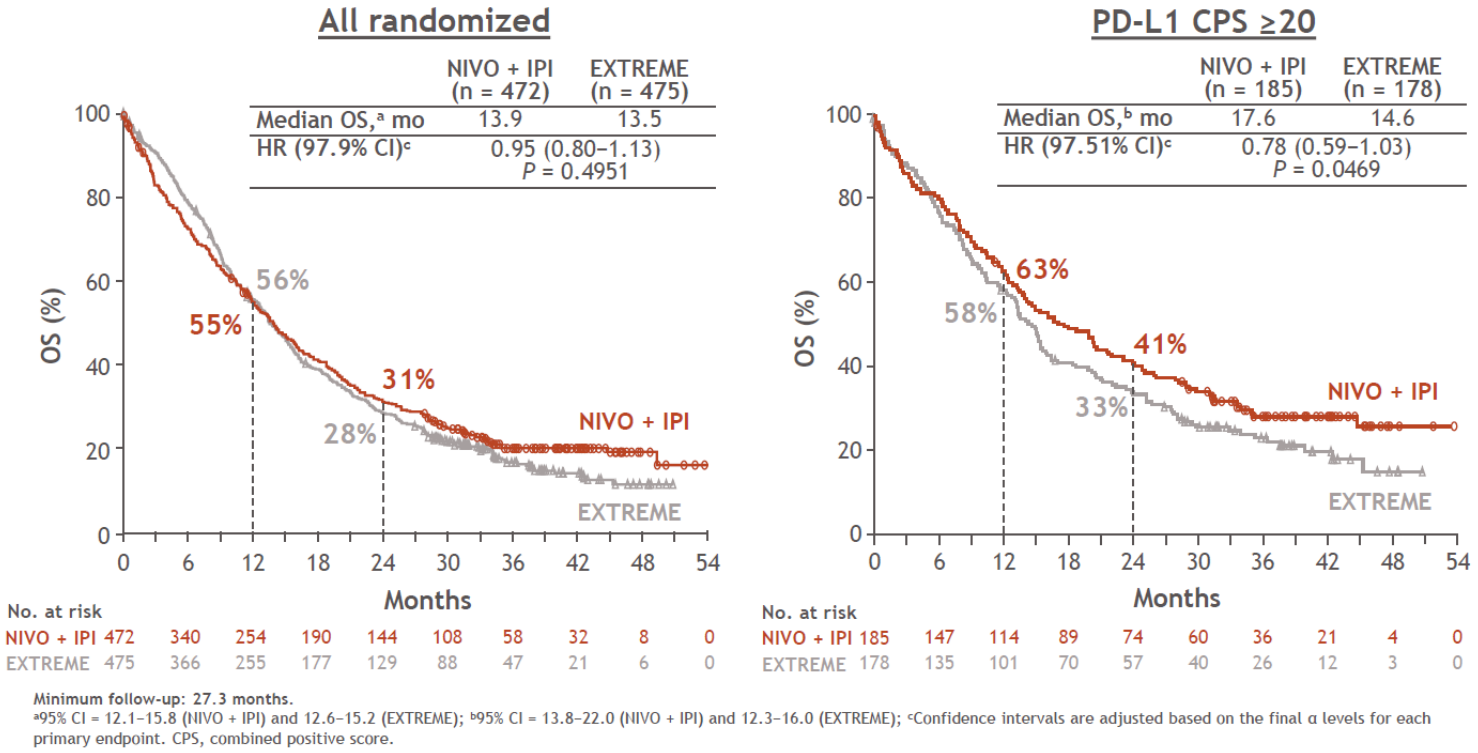
ORL

LBA36 - Nivolumab (N) + ipilimumab (I) vs EXTREME as first-line (1L) treatment (tx) for recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN)

CheckMate 651: 1L NIVO + IPI in R/M

Primary endpoints: OS with NIVO + IPI vs EXTREME



Minimum follow-up: 27.3 months.
[a]95% CI = 12.1–15.8 (NIVO + IPI) and 12.6–15.2 (EXTREME); [b]95% CI = 13.8–22.0 (NIVO + IPI) and 12.3–16.0 (EXTREME); [c]Confidence intervals are adjusted based on the final α levels for each primary endpoint. CPS, combined positive score.

- Efficace sur ORR (≥1 ou ≥20)
- OS: PDL1 ≥1 et 1-19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