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MEETING SUMMARY: TRK FUSION-POSITIVE CANCER FROM WCLC, ECP AND ESMO 2022

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SEPTEMBER 2022

DISCLOSURES

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This content is supported by an independent educational grant from Bayer.

Disclosures: Dr Fernando Santini has received honoraria from Bayer

SELECTED ABSTRACTS FROM WCLC, ECP AND ESMO 2022

- **Updated clinical efficacy and safety data from larotrectinib:**
  - 463P - Efficacy and safety of larotrectinib in a pooled analysis of patients (pts) with tropomyosin receptor kinase (TRK) fusion cancer with an extended follow-up. Presented by R.S. McDermott (ESMO 2022)
  - EP08.02-148 - Extended follow-up of efficacy and safety of larotrectinib in patients with TRK fusion lung cancer. Presented by V. Moreno (WCLC 2022)

- **Promising testing methods:**
  - OFP-12-007: Ultra-fast gene fusion assessment as a reflex testing in daily clinical practice for advanced non-small cell lung cancer patients. Presented by C. Bontoux (ECP 2022)

TRK, tropomyosin receptor kinase

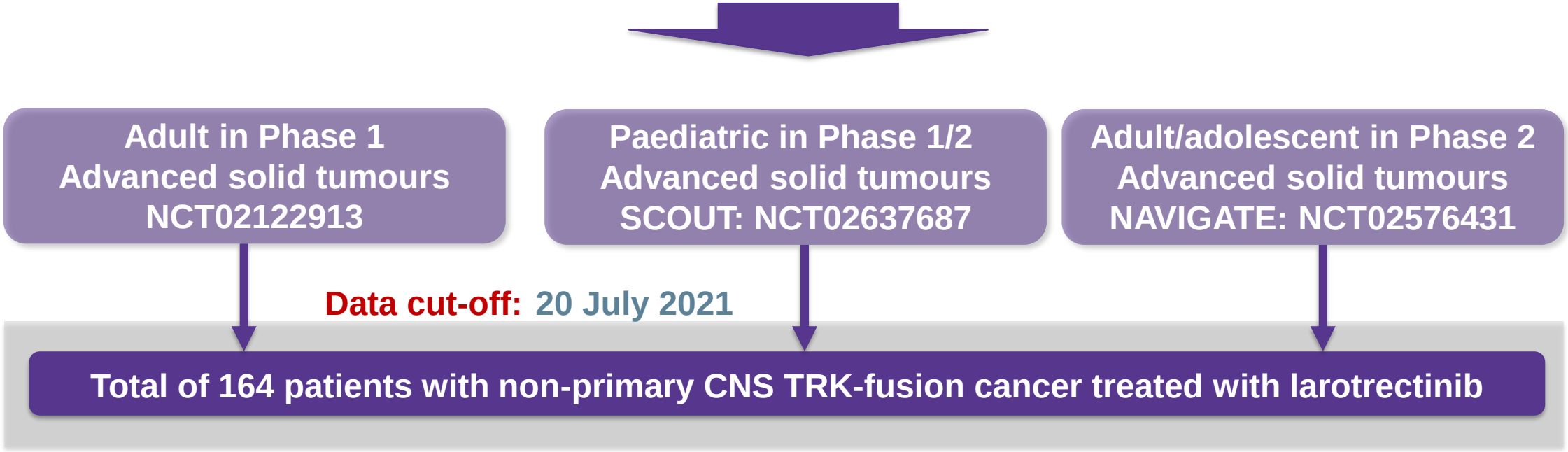
EFFICACY AND SAFETY OF LAROTRECTINIB IN A POOLED ANALYSIS OF PATIENTS WITH TRK FUSION CANCER WITH AN EXTENDED FOLLOW-UP

McDermott RS, et al. ESMO 2022. Abstract #463P

TRK, tropomyosin receptor kinase

BACKGROUND

larotrectinib = first-in-class, highly selective, CNS-active TRK inhibitor approved to treat adult and paediatric patients with TRK fusion cancer

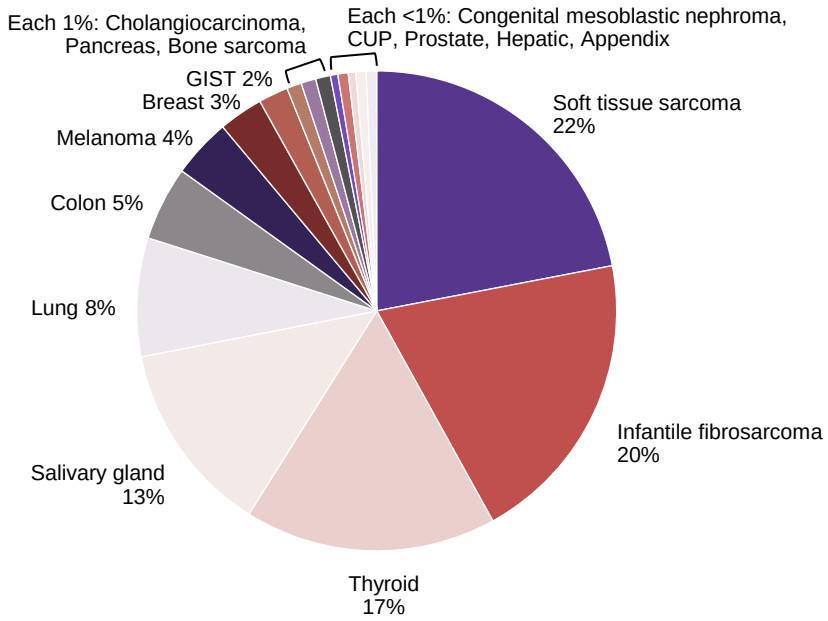


McDermott RS, et al. ESMO 2022. Abstract #463P

CNS, central nervous system; TRK, tropomyosin receptor kinase

INTEGRATED DATASET: HIGH ORR ACHIEVED WITH LAROTRECTINIB ACROSS VARIOUS TUMOURS

PATIENT POPULATION BY TUMOUR TYPE (N=164)



EFFICACY ASSESSMENTS

	Overall	Patients with CNS metastases
Evaluable patients, n	164	14
ORR (95% CI), %	74 (67-81)	86 (57-98)
Best response, n (%)		
Complete response	40 (24)	1 (7)
Pathological complete response	10 (6)	0
Partial response	72 (44)	11 (79)
Stable disease	22 (13)	1 (7)
Progressive disease	13 (8)	0
Not determined[a]	7 (4)	1 (7)

[a] Patients who discontinued study drug without evaluable post-baseline assessments

McDermott RS, et al. ESMO 2022. Abstract #463P

CI, confidence interval; CNS, central nervous system; CUP, cancer of unknown primary; GIST, gastrointestinal stromal tumour; ORR, objective response rate

EFFICACY: DoR, PFS, AND OS IN PATIENTS WITH TRK FUSION CANCER

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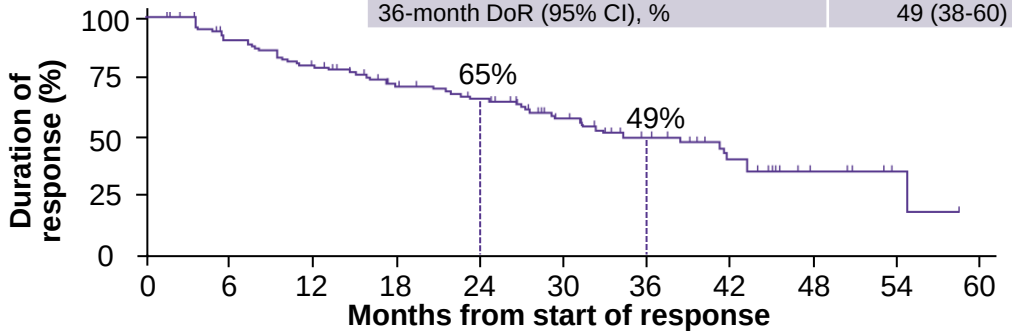
DoR

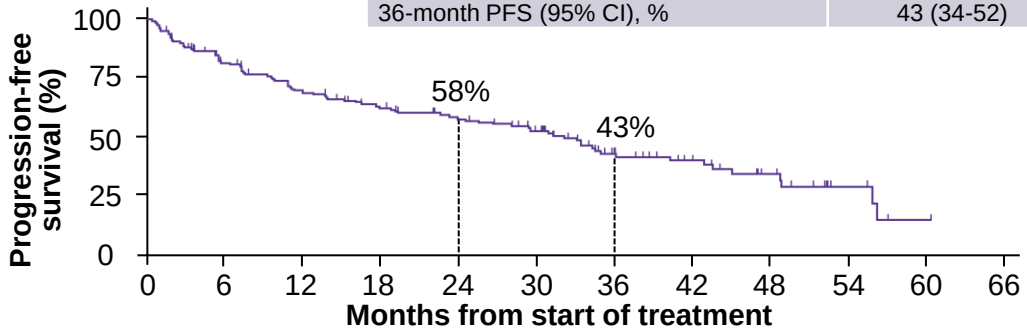
Median DoR (95% CI), months	34.5 (27.6-43.3)
Median follow-up, months	34.1
24-month DoR (95% CI), %	65 (56-75)
36-month DoR (95% CI), %	49 (38-60)



No. at risk	122	100	87	69	60	40	26	16	6	2	0

PFS

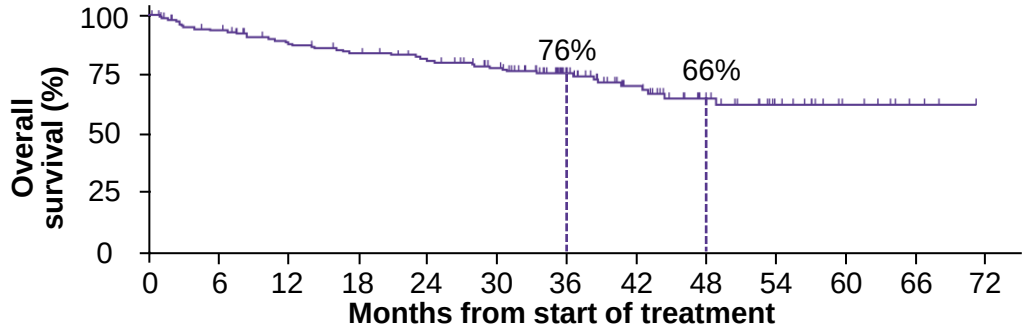
Median PFS (95% CI), months	32.0 (23.4-40.2)
Median follow-up, months	35.8
24-month PFS (95% CI), %	58 (50-66)
36-month PFS (95% CI), %	43 (34-52)



No. at risk	164	121	98	84	71	58	31	22	14	5	1	0

OS

Median OS (95% CI), months	Not reached (NE-NE)
Median follow-up, months	38.0
36-month OS (95% CI), %	76 (69-83)
48-month OS (95% CI), %	66 (57-75)

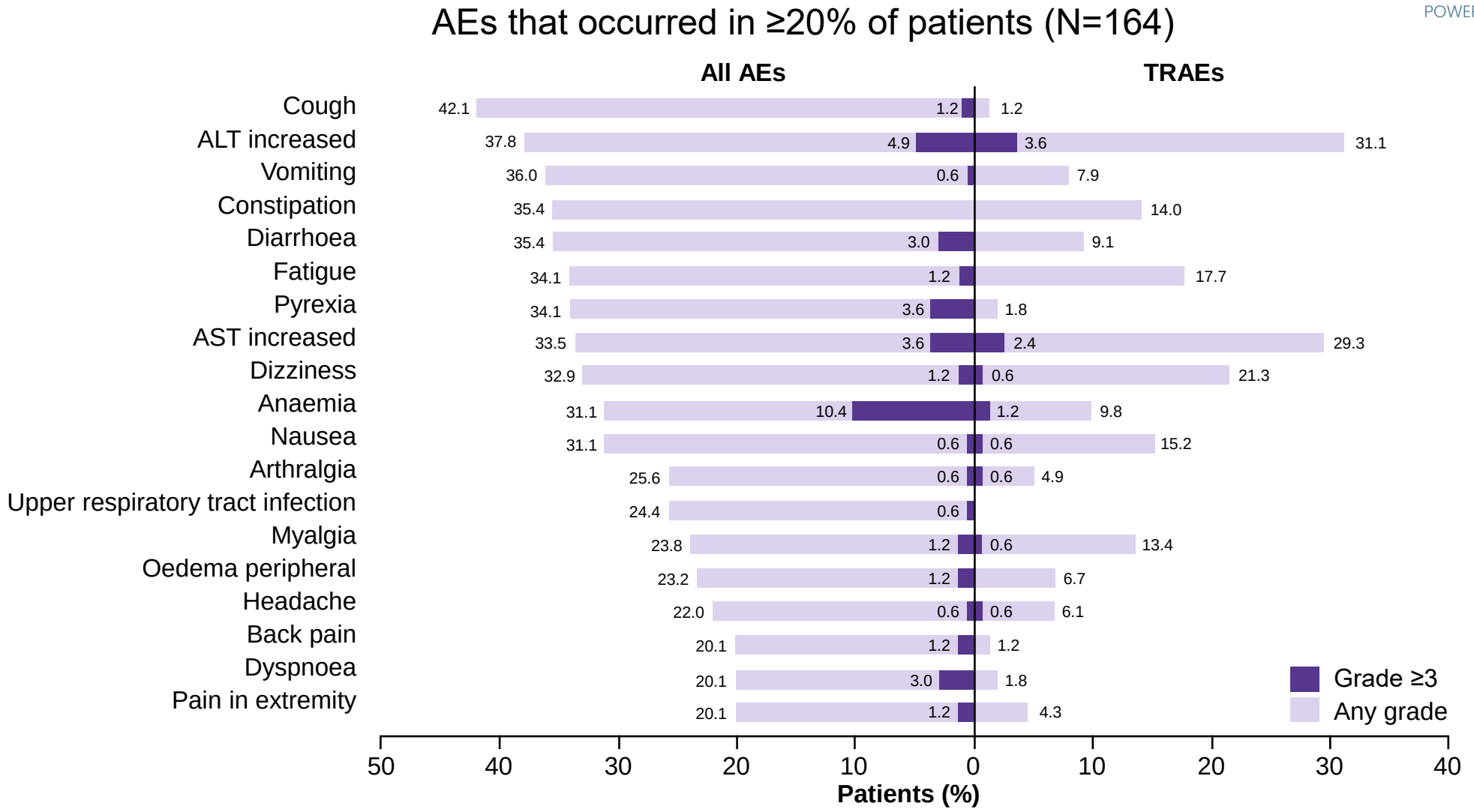


No. at risk	164	147	133	124	115	102	69	47	30	17	8	3	0

McDermott RS, et al. ESMO 2022. Abstract #463P

CI, confidence interval; DoR, duration of response; NE, not estimable; No., number; OS, overall survival; PFS, progression-free survival; TRK, tropomyosin receptor kinase

SAFETY: NO NEW SIGNAL IDENTIFIED



McDermott RS, et al. ESMO 2022. Abstract #463P

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event

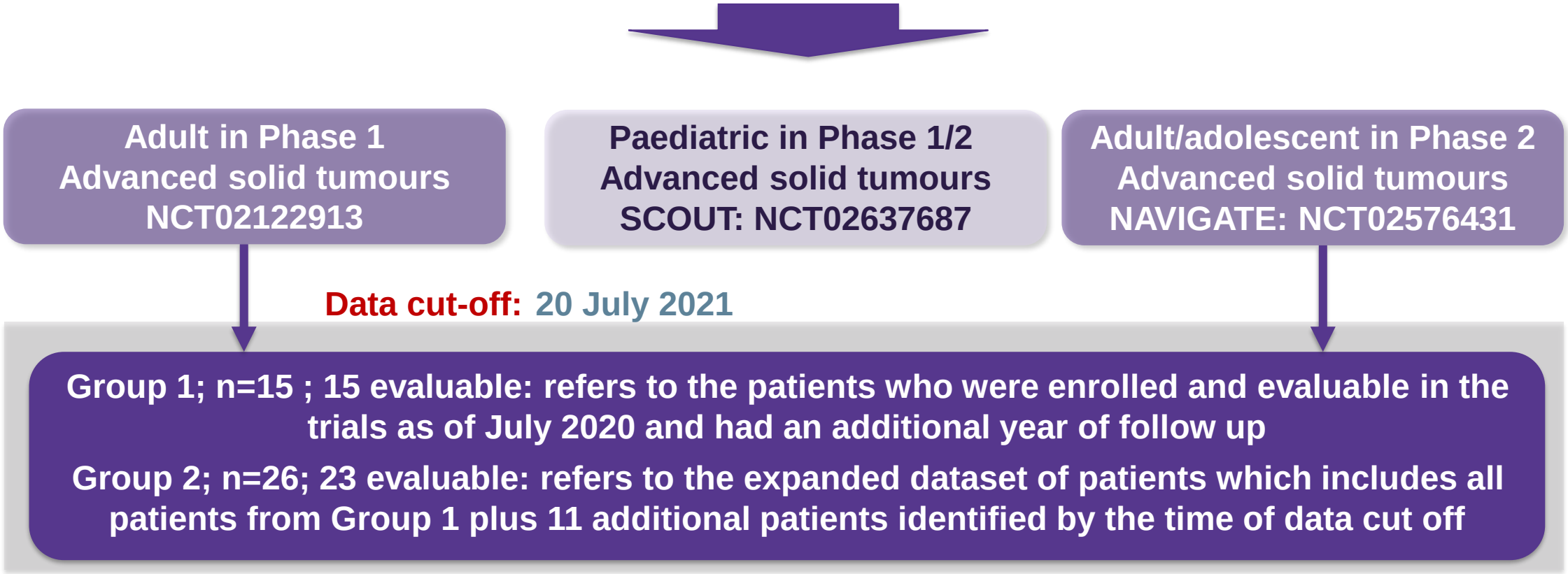
EXTENDED FOLLOW-UP OF EFFICACY AND SAFETY OF LAROTRECTINIB IN PATIENTS WITH TRK FUSION LUNG CANCER

Moreno V, et al. WCLC 2022. Abstract #EP08.02-148

TRK, tropomyosin receptor kinase

BACKGROUND

larotrectinib = first-in-class, highly selective, CNS-active TRK inhibitor approved to treat adult and paediatric patients with TRK fusion cancer



Moreno V, et al. WCLC 2022. Abstract #EP08.02-148

CNS, central nervous system; TRK, tropomyosin receptor kinase

KEY EFFICACY RESULTS IN PATIENTS WITH TRK FUSION LUNG CANCER

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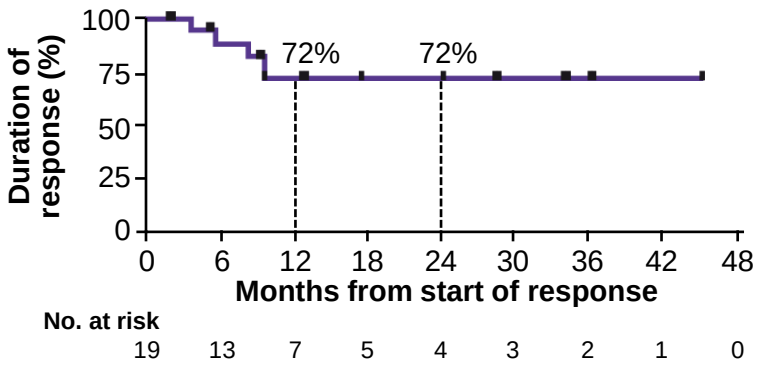
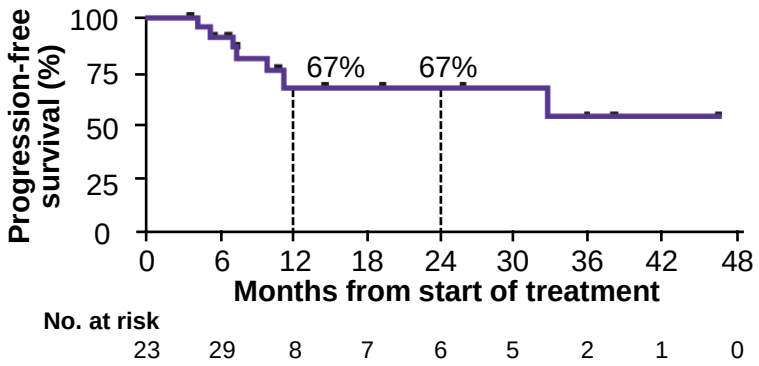
Efficacy from the Group 1 and Group 2 datasets

	Patients from the Group 1 dataset	Patients from the Group 2 dataset
IRC evaluable patients, n	15	23
ORR (95% CI), %	87 (60-98)	83 (61-95)
Best overall response, n (%)		
Complete response	2 (13)	2 (9)
Partial response	11 (73)	17 (74)
Stable disease	2 (13)	4 (17)
Progressive disease	0	0

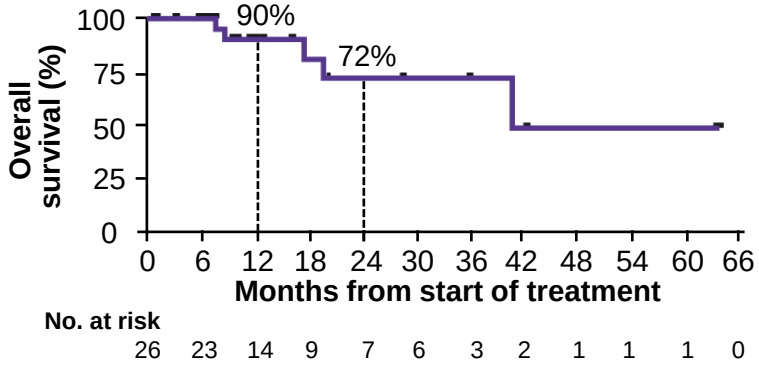
DoR, PFS and OS in patients with TRK fusion lung cancer from the Group 2 dataset (n=26)



Median DoR (95% CI), months	Not reached
Median follow-up, months	12.9
12-month DoR (95% CI), %	72 (48-96)
24-month DoR (95% CI), %	72 (48-96)



Median PFS (95% CI), months	Not reached
Median follow-up, months	14.6
12-month PFS (95% CI), %	67 (44-90)
24-month PFS (95% CI), %	67 (44-90)



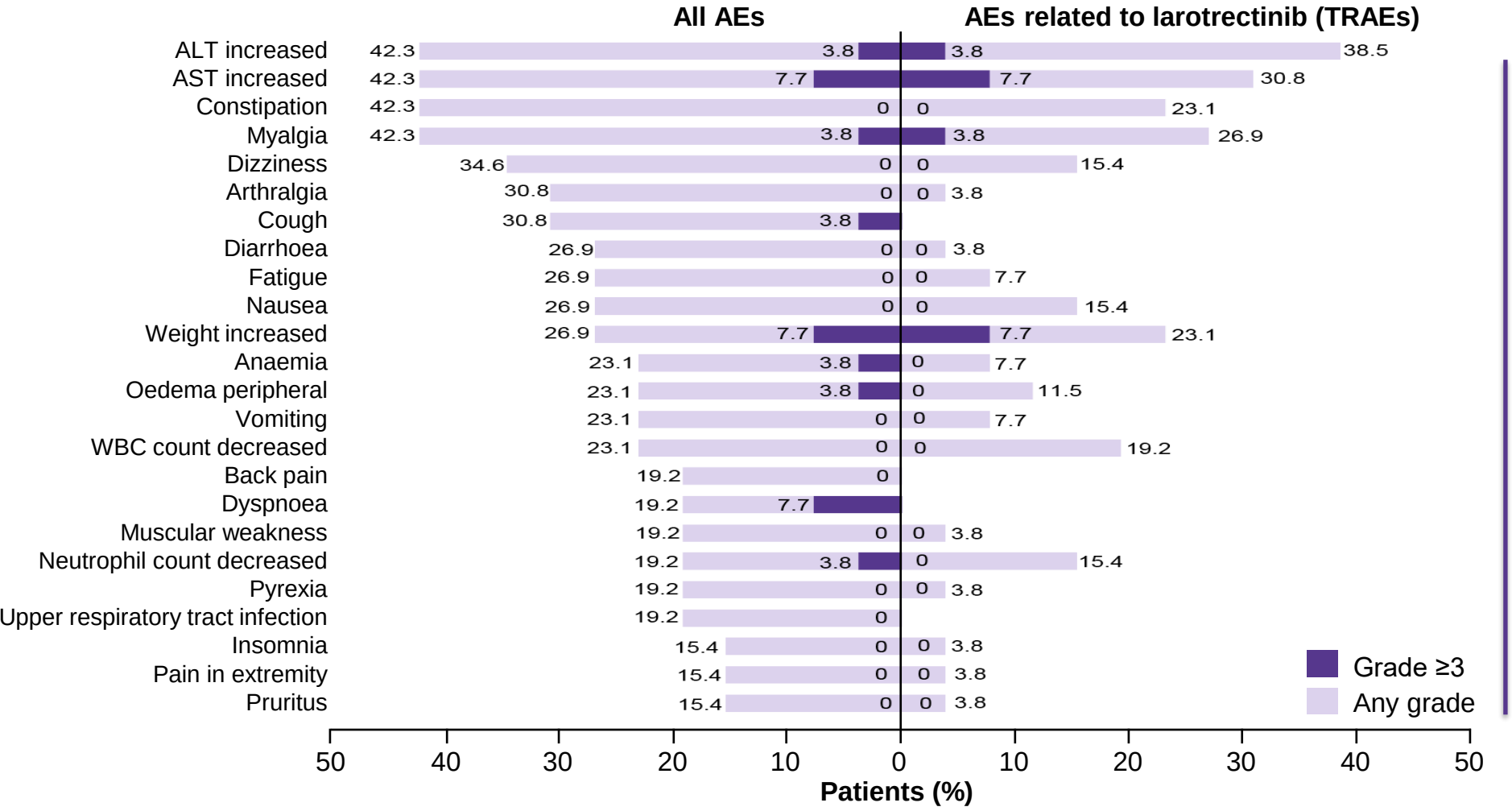
Median OS (95% CI), months	40.7 (19.4-NE)
Median follow-up, months	12.9
12-month OS (95% CI), %	90 (78-100)
24-month OS (95% CI), %	72 (48-97)

Moreno V, et al. WCLC 2022. Abstract #EP08.02-148

CI, confidence interval; DoR, duration of response; IRC, independent review committee; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression free survival; TRK, tropomyosin receptor kinase

SAFETY: NO NEW SAFETY SIGNALS IDENTIFIED

AEs occurring in >/=15% of patients from Group 2 (n=26)



For the Group 1 dataset:

- with an additional year of follow-up, there were no new safety signals identified

Moreno V, et al. WCLC 2022. Abstract #EP08.02-148

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment related adverse event; WBC, white blood cell

ULTRA-FAST GENE FUSION ASSESSMENT AS A REFLEX TESTING IN DAILY CLINICAL PRACTICE FOR ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS

Bontoux C, et al. ECP 2022. Abstract #OFP-12-007

BACKGROUND & METHODS

- **Objectives**:
  - There is an urgent need to improve the broad molecular profiling (reflex testing) of advanced non-squamous non-small cell lung carcinoma patients, notably for a rapid assessment of multiple genomic alterations

- **Methods:**
  - We compared two ultra-fast gene fusion assessment assays, using a next generation sequencing (Genexus, Oncomine™ Precision Assay, Thermo-Fisher) or an RT-PCR (Idylla™, GeneFusion Assay, Biocartis) approach, for reflex testing at diagnosis

Bontoux C, et al. ECP 2022. Abstract #OFP-12-007

RT-PCR, reverse transcription polymerase chain reaction

RESULTS AND CONCLUSION

- 250 NS-NSCLC patients (68 *ALK*, 26 *ROS1*, 15 *RET*, 6 *NTRK*, 11 *MET* positive and 125 wild type patients) from eight centres were included; 83% of patients were stage IIIB-IV

- The sensitivity (98%) and specificity (99%) of the two approaches were analogous, when compared to gold standard methods, accredited according to the ISO 15189 norm

Conclusion: Ultra-fast gene fusion evaluation using NGS or RT-PCR approaches should be developed as a reflex testing for NS-NSCLC at diagnosis in order to treat these patients according to international recommendations and guidelines

Bontoux C, et al. ECP 2022. Abstract #OFP-12-007

ALK, anaplastic lymphoma kinase; ISO, International Organisation for Standardization; *MET*, MET proto-oncogene; NGS, next-generation sequencing; NS-NSCLC, non-squamous non-small cell lung carcinoma; *NTRK*, neurotrophic receptor tyrosine kinase; *RET*, RET proto-oncogene; *ROS1*, ROS proto-oncogene 1; RT-PCR, reverse transcription polymerase chain reaction

CONCLUSIONS

CONCLUSIONS

- **First generation TRK inhibitor:**
  - larotrectinib continues to demonstrate a robust clinical efficacy with a manageable safety profile in various solid tumour types including in lung cancer

- **Testing for presence of *NTRK* fusions:**
  - Presence of *NTRK* fusions must be tested for in order to identify patients who can benefit from first-generation TRK inhibitors such as larotrectinib and entrectinib
  - A reflex testing method is valuable for efficient and rapid identification (within 1 day) of patients with *NTRK* positive tumours

NTRK, neurotrophic receptor tyrosine kinase; TRK, tropomyosin receptor kinase

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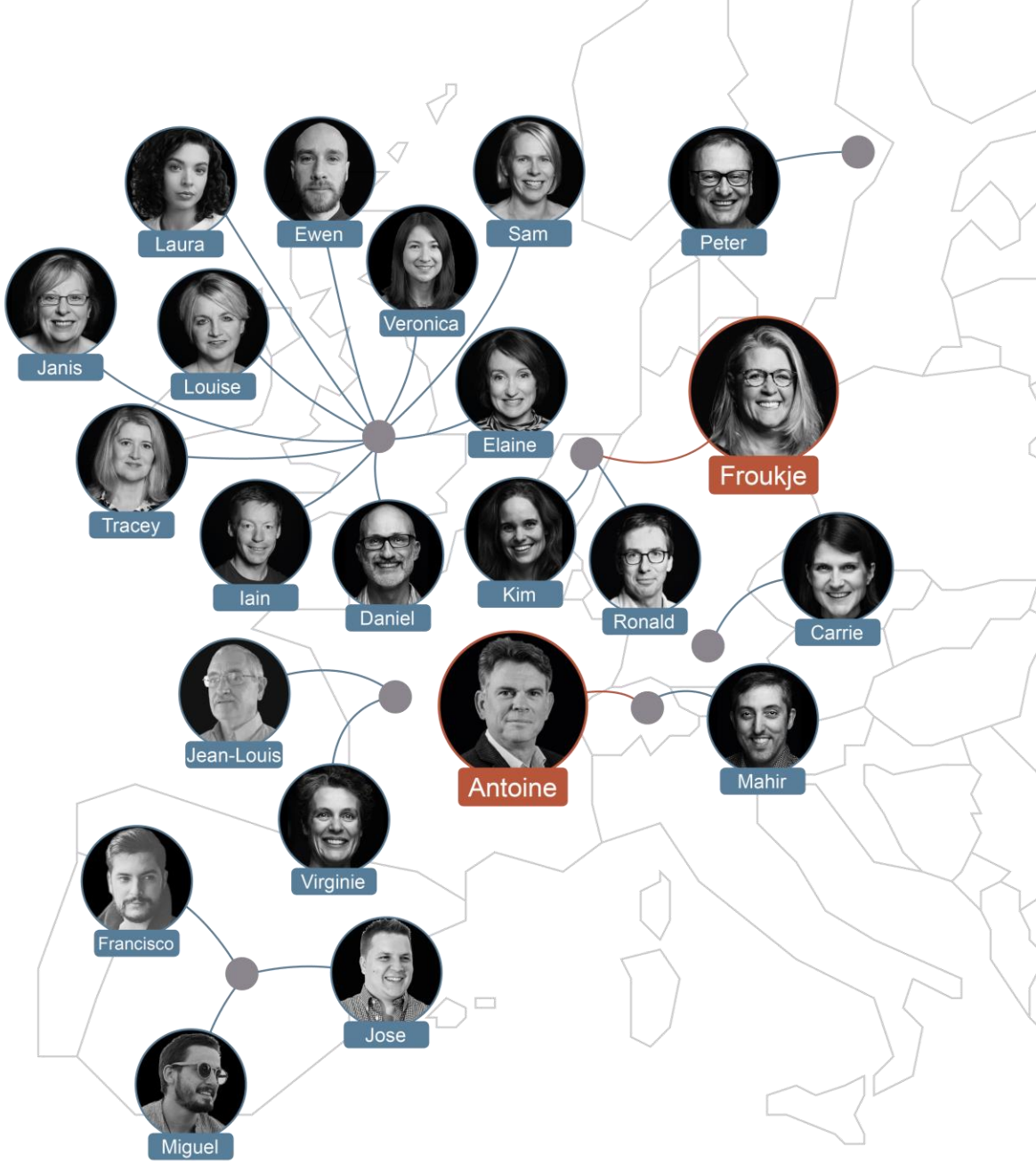

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