



# Federated analysis of overall survival (OS) by location of metastasis in patients with metastatic non-small cell lung cancer (mNSCLC) from the Digital Oncology Network for Europe (DigiONE)

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## Introduction

- Non-small cell lung cancer (NSCLC) is usually diagnosed in stage IV, with a median overall survival typically less than one year.
- This survival period can range from a few months to several years, depending on molecular characteristics, treatment received and patient characteristics.
- DigiONE integrated core variables into local Observational Medical Outcomes Partnership (OMOP) databases to create the first European pan-cancer hospital network using OMOP.
- With maintained databases and reproducible analytical approaches, research centres aim to generate faster precision oncology Real World Evidence (RWE).
- These preliminary results of OS by locations of metastasis in mNSCLC are a first step to studying routine treatment received and additional outcomes.

## Methods

- Retrospective routine care data from OMOP databases at three centers (Leeds, Maastricht, Oslo) were collected for patients diagnosed with de novo or recurrent/refractory mNSCLC between 1 Nov 2018 and 30 Sep 2022.
- Patient characteristics were described at index, i.e. mNSCLC diagnosis date.
- Kaplan-Meier (KM) curves for OS from index were plotted for the overall cohort, and for patient subgroups by metastasis location as follows:
  - Brain only [A]
  - Bone only [B]
  - Lung or pleura only [C]
  - Liver only<sup>†</sup>
  - Adrenal gland only<sup>†</sup>
  - Other single or multiple locations (not including brain, bone, lung, adrenal gland and liver) [D]
  - Multiple locations including brain (brain + any other location) [E]
  - Multiple listed locations excluding brain (at least one of bone/lung/adrenal gland/liver + any other non-brain location) [F]
- <sup>†</sup> Due to small patient counts (N<10) in the subgroup, KM estimates are not presented individually for the subgroup

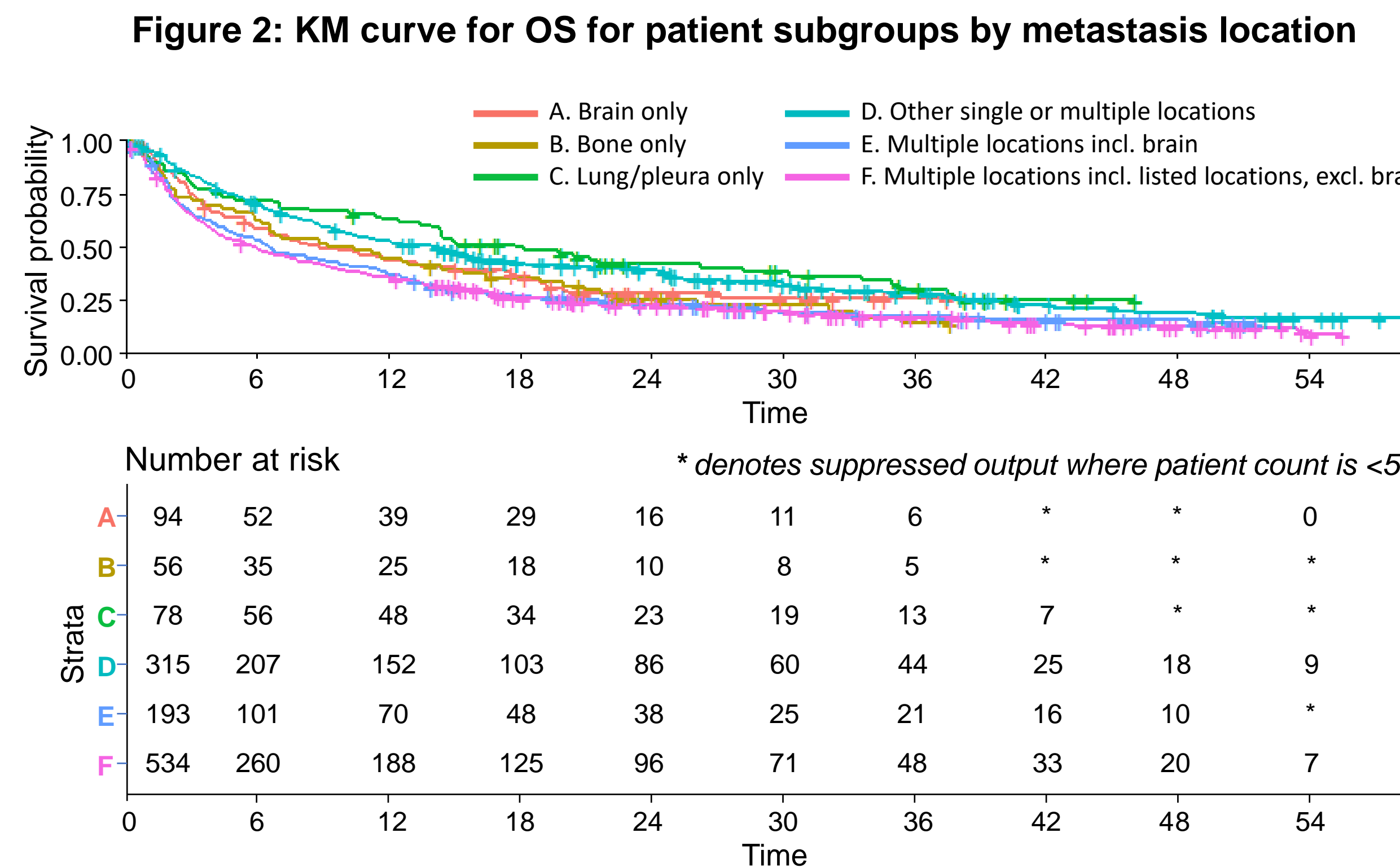
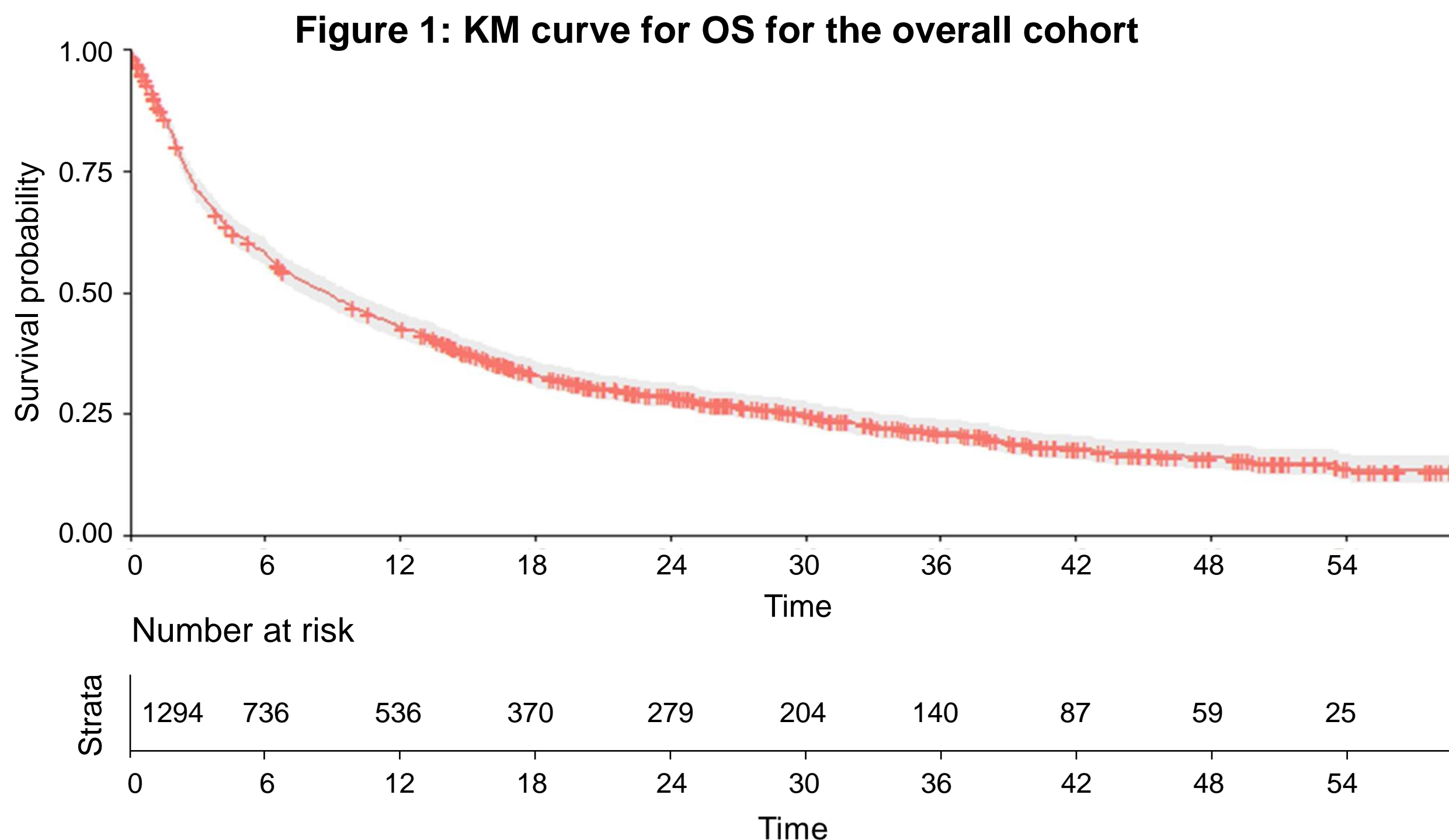
- A federated learning approach with Vantage6 was used, operating on Gaussian-noised individual survival time to further reduce risk of patient reidentification<sup>1</sup>.

## Results

- The analysis included a total of 1,294 patients with mNSCLC, encompassing those who received systemic anti-cancer therapy (SACT) and those who did not.
- Table 1** summarises all patients' age, sex, presentation of metastatic disease at index. Within the overall cohort, median age at index was 70 years, 53% were male, and 73% patients had metastatic disease at primary NSCLC diagnosis.
- The median OS (mOS) for the overall cohort was 8.7 months as shown in **Figure 1**. The survival probability (95% CI) of patients at 6, 12, 18 and 24 months are illustrated in **Table 2**.
- In subgroups of metastatic location (**Figure 2** and **Table 3**), patients with multiple metastasis locations without brain metastasis (BM) [F] had the shortest mOS of 5.88 months, followed by those with multiple metastasis locations including BM [E, mOS = 6.6 months], and those with brain metastasis only [A, mOS = 8.84 months].
- In contrast to [F], patients with contralateral lung or pleura only metastasis [C] had the longest mOS of 17.81 months, p=0.001, logrank test in **Table 4**.

**Table 1: Patient characteristics at index**

Patient characteristics		Overall cohort N = 1294	Leeds N = 600	Maastricht N = 363	Oslo N = 331
<b>Age</b>	Median	70	70	69	70
<b>Sex</b>	Male	683 (53%)	309 (52%)	195 (54%)	179 (54%)
	Female	611 (47%)	291 (49%)	168 (46%)	152 (46%)
<b>Metastatic disease presentation</b>	De novo	949 (73%)	441 (74%)	301 (83%)	207 (63%)
	Recurrence / refractory	345 (27%)	159 (27%)	62 (17%)	124 (37%)



**Table 3: Median OS (mOS) and survival probability (95% CI) of patients at 6 – 24 months timepoints of patient subgroups by metastasis location**

Patient subgroups	A. Brain only N = 94 (7.3%)	B. Bone only N = 56 (4.3%)	C. Lung / pleura only N = 78 (6.0%)	D. Other single / multiple locations N = 315 (24.3%)	E. Multiple locations incl. brain N = 193 (14.9%)	F. Multiple listed locations excl. brain N = 534 (41.3%)
	<b>mOS (Q1 – Q3)</b>	8.84 (3.12 – NA)	9.82 (2.27 - 26.05)	17.81 (3.91 - 37.85)	14.16 (4.6 - 39.75)	6.6 (2.07 - 20.34)
<b>Timepoint</b>	Number of patients Survival probability (95% CI)					
<b>6 Months</b>	52 58.5 (47.7, 67.8)	35 62.5 (48.5, 73.7)	56 71.8 (60.4, 80.4)	207 70.5 (65.0, 75.4)	101 53.2 (45.9, 60.0)	260 49.1 (44.8, 53.2)
<b>12 Months</b>	39 43.9 (33.5, 53.8)	25 44.6 (31.4, 57.0)	48 62.8 (51.0, 72.4)	152 52.6 (46.8, 58.2)	70 36.9 (30.1, 43.7)	188 35.5 (31.4, 39.6)
<b>18 Months</b>	29 35.8 (26.0, 45.7)	18 35.5 (23.2, 47.9)	34 49.5 (38.0, 60.1)	103 41.9 (36.2, 47.6)	48 26.6 (20.5, 33.1)	125 26.2 (22.5, 30.1)
<b>24 Months</b>	16 28.0 (18.9, 37.8)	10 25.2 (14.5, 37.4)	23 42.0 (30.7, 52.9)	86 39.0 (33.2, 44.7)	38 23.1 (17.4, 29.4)	96 22.5 (19.0, 26.2)

**Table 2: Median OS (mOS) and survival probability (95% CI) of patients at 6 – 24 months timepoints of the overall cohort**

Overall cohort N=1294	
<b>mOS (Q1 – Q3)</b>	8.7 (2.6 – 29.8)
<b>Timepoint</b>	Number of patients Survival probability (95% CI)
<b>6 Months</b>	736 58.4 (55.7, 61.1)
<b>12 Months</b>	536 42.9 (40.3, 45.7)
<b>18 Months</b>	370 33.1 (30.6, 35.9)
<b>24 Months</b>	279 28.7 (26.3, 31.4)

**Table 4: Pairwise logrank test by metastasis location**

Pairwise logrank test (p-value)	A. Brain only	B. Bone only	C. Lung / pleura only	D. Other single / multiple locations	E. Multiple locations incl. brain	F. Multiple listed locations incl. brain
<b>B. Bone only</b>	0.61	NA	NA	NA	NA	NA
<b>C. Lung/pleura only</b>	0.194	0.11	NA	NA	NA	NA
<b>D. Other single/multiple locations</b>	0.244	0.194	0.515	NA	NA	NA
<b>E. Multiple locations incl. brain</b>	0.194	0.538	<b>0.005</b>	<b>0.001</b>	NA	NA
<b>F. Multiple listed locations excl. brain</b>	0.11	0.334	<b>0.001</b>	<b>0.001</b>	0.61	0.61

*P-value in bold denotes statistically significant comparison*

## CONCLUSION

- The curation, standardisation, and harmonisation of routine care data across hospitals is an arduous task due to its often unstructured, incomplete, and dissimilar nature. Overcoming this challenge can facilitate faster collaborations aiming at reliable RWE research.
- Comparable key findings from the current study with previous trials and retrospective analyses reflect the accuracy of our approach. Our key findings include:
  - Over the study period (Nov 2018 – Sep 2022), an average of 73% of the total patients were first diagnosed at the metastatic stage<sup>2</sup>.
  - The most common metastatic locations were studied. Over half of the study cohort were found to have metastasised to more than one of these locations, and their mOS were comparatively shorter than other subgroups<sup>3</sup>.
  - There is no statistical significance difference in patients with multiple metastatic locations with and without BM<sup>4</sup>.
- Future analyses will assess OS and time to next treatment by the first and second line of therapy prescribed including adjustment for prognostic characteristics.

## References

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## Acknowledgement

- This work is part of the DIGICORE pan-European research network comprised of academic cancer centres and two industrial members (IQVIA and Illumina).
- The DigiONE project was funded by IQVIA and Illumina.
- Medical writing support was provided by Junaid A Khan, senior medical writer and project management by Jie Yeap, senior consultant at IQVIA.