CONFLICT OF INTEREST DISCLOSURE

Disclosure. All authors report no conflicts of interest in this work.

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Use of Real-World Big Data To Assess The Effectiveness on Overall Survival Among Chemotherapy or Immunotherapy in First Line Metastatic Non-Small Cell Lung Carcinoma Patients in an Italian Setting

Degli Esposti L[1], Sangiorgi D[1], Ancona DD[2], Andretta M[3], Barbieri A[4], Bartolini F[5], Cavaliere A[6], Chinellato A[7], Ciaccia A[8], Cillo M[9], Citraro R[10], Costantini A[11], De Francesco A[10], Dell'Orco S[12], Di Manno G[12] Ferrante F[13], Gentile S[14], Lavalle A[14], Moscogiuri R[15] Pastorello M[16] Procacci C[2], Re D[17], Santoleri F[11], Ubertazzo L[18], Vercellone A[19], **Perrone V[1]**

[1]CliCon S.r.l., Health, Economics & Outcomes Research, Bologna, Italy; [2]ASL BAT, Andria (BT), Italy; [3]Azienda ULSS 8 Berica, Vicenza, Italy; [4]ASL Vercelli, Vercelli, Italy; [5]USL Umbria 2, Terni, Italy; [6]ASL Viterbo, Viterbo, Italy; [7]Azienda ULSS 3 Serenissima, Mestre (VE), Italy; [8]ASL Foggia, Foggia, Italy; [9]ASL Salerno, Salerno, Italy; [10]Dipartimento di Scienze della Salute, Università Magna Grecia di Catanzaro, Catanzaro, Italy; [11]ASL Pescara, Pescara, Italy; [12] UOC Farmaceutica Territoriale, ASL Roma 6, Albano Laziale RM, Italy; [13]ASL Frosinone, Frosinone, Italy; [14]Direzione Generale per la Salute Regione Molise, Campobasso, Italy; [15]ASL Taranto, Taranto, Italy; [16]ASP Palermo, Palermo, Italy; [17]ASL Teramo, Teramo, Italy; [18]ASL Roma 4, Civitavecchia (RM), Italy; [19]ASL Napoli 3 SUD, Torre del Greco (NA), Italy

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Presenting:
Melania Dovizio[1]

BACKGROUND AND OBJECTIVES

- In oncology, **big data analysis** has been gaining increasing interest in recent years, as these data allow for the generation of evidence to address many of the questions arising in cancer care, using the information of **the real clinical practice** [1].
- Investigations based on **real-world evidence** can provide data for understanding outcomes in patients under specific medication, to better guide **treatment decisions** in the routine care [2].
- The treatment landscape for metastatic advanced non-small cell lung cancer (**met NSCLC**) has evolved rapidly since immuno-oncology (I/O) therapies were introduced [3], and currently only limited real-world data are available to assess the impact of I/O therapy respect to the standard of care chemotherapy on outcomes in met NSCLC patients, in Italy.
- **The aim of the present study was to assess the overall survival of metastatic NSCLC patients receiving chemotherapy or immunotherapy as first line by using real-world data in a sample population in Italy.**

References:
[1] Di Maio M et al., Oncologist. 2020 May;25(5):e746-e752
[2] Sherman RE et al., N Engl J Med 2016;375:2293–229
[3] Steuer CE, et al., JCO Oncol Pract. 2021 25:OP2100305.

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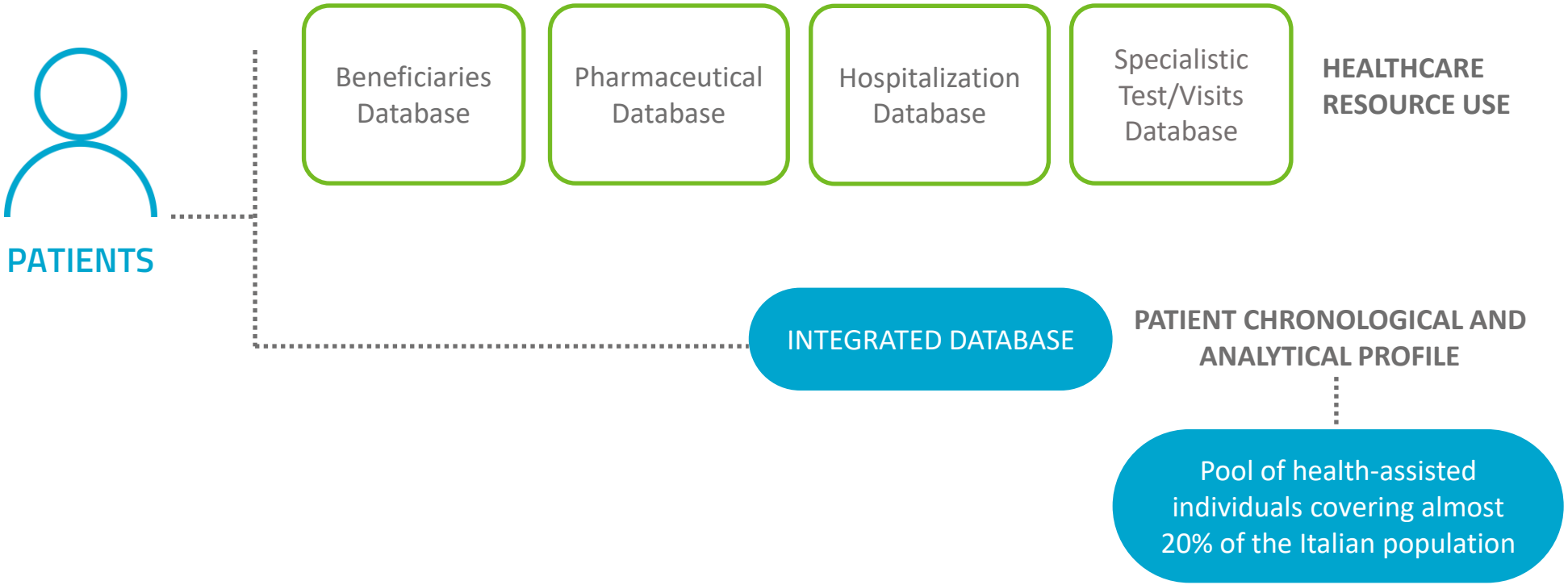
METHODS – DATA SOURSE

ADMINISTRATIVE DATABASE

A ***retrospective study*** was conducted using ***administrative databases*** from a sample of Italian Local Health Units. Specifically, administrative flows contain all the information regarding the healthcare resources/services reimbursed by the Italian National Healthcare Service.



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"The integration of administrative datasets makes it possible to represent the patient's entire clinical history and not just individual prescriptions. The analyzes were conducted on exclusively anonymous data in full compliance with privacy regulations. Clicon s.r.l. has obtained the approval as per legislation by all the Ethics Committees to analyze these data. The results are exclusively in aggregated form and never attributable to a single institution, department, doctor, individual, or individual prescribing behaviors. The study was conducted in full compliance with current legislation for retrospective studies."

METHODS-STUDY DESIGN
STUDY POPULATION AND STUDY PERIODS

Study Population:
20% of the Italian population

- at least **one hospitalization with discharge diagnosis of lung cancer** and with aspecific chemoterapy (CT)* and without antineoplastic drugs indicated for met NSCLC **OR**
- at least **one prescription for antineoplastic drugs** (targeted therapy, immunotherapy, I/O) indicated for met NSCLC

INCLUSION CRITERIA

Based on the type of drug prescribed, the patients were divided into:

 **aspecific CT**

 **I/O Pembrolizumab**

STUDY POPULATION

All patients with at least *one hospitalization OR at least one prescription for antineoplastic drugs* indicated for Metastatic NSCLC between January 2017 and December 2018 (*inclusion period*) were identified. Among those, only patients starting **a first line treatment** with aspecific CT* or I/O Pembrolizumab** were included.

STUDY PERIODS

Index-date: first antineoplastic prescription

Follow-up: all available period (at least 2 ys)

Characterization: all available period before index date.

**Chemotherapy was evaluated by the presence of inpatient/outpatient procedures (DRG 410, or procedures codes 99.25, 99.28, 99.29) or treatments with pemetrexed or other antineoplastic drugs (excluding immunotherapy drugs and targeted therapy)*

***PEMBROLIZUMAB (ATC code: L01XC18): patients without diagnosis of melanoma [(ICD-9-CM code: 172, V10.82 OR treatment with ipilimumab (ATC code: L01XC11), dabrafenib (ATC code: L01XE23), vemurafenib (ATC code: L01XE15), cobimetinib (ATC code: L01XE38), dacarbazine (L01AX04)] AND with diagnosis of Lung Cancer OR Chest RX (code: 87.44.1) OR Chest CT scan (code: 87.41.1) OR Chest MRI (code: 88.92.1) OR Fiberoptic bronchoscopy (code:33.22) bronchial biopsy (code:33.24) AND PET (codes 92.11.8, 92.19.8, 92.09.1, 92.11.7, 92.18.6)*

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RESULTS-BASELINE CHARACTERISTICS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF met NSCLC PATIENTS IN FIRST LINE TREATMENT

- A TOTAL OF **3,126** (MEAN AGE 68.6 YEARS, 68.2% MALE) AND **316** (MEAN AGE 68.6 YEARS, 74.4% MALE) **MET-NSCLC PATIENTS** IN FIRST-LINE TREATMENT WITH **ASPECIFIC CT** OR **I/O-PEMBROLIZUMAB**, RESPECTIVELY, WERE INCLUDED.

- IN BOTH GROUPS, METASTASES WERE LOCATED MORE FREQUENTLY IN **BONES** (25.8% ASPECIFIC CT, 14.9% I/O), **BRAIN** (18.3% ASPECIFIC CT, 10.1% I/O), AND **RESPIRATORY TRACT** (29.6% ASPECIFIC CT, 20.9% I/O).

	aspecific CT N=3,126	I/O-pembrolizumab N=316
Age, mean (SD)	68.6 (9.8)	68.6 (9.7)
Male, n(%)	2,131 (68.2)	235 (74.4)
Sites of metastasis		
Brain, n (%)	571 (18.3)	32 (10.1)
Bones, n (%)	807 (25.8)	47 (14.9)
Liver, n (%)	522 (16.7)	14 (4.4)
Respiratory tract, n (%)	926 (29.6)	66 (20.9)
Adrenal glands, n (%)	222 (7.1)	16 (5.1)
Peritoneum, n (%)	76 (2.4)	6 (1.9)
Other sites, n (%)	204 (6.5)	19 (6.0)

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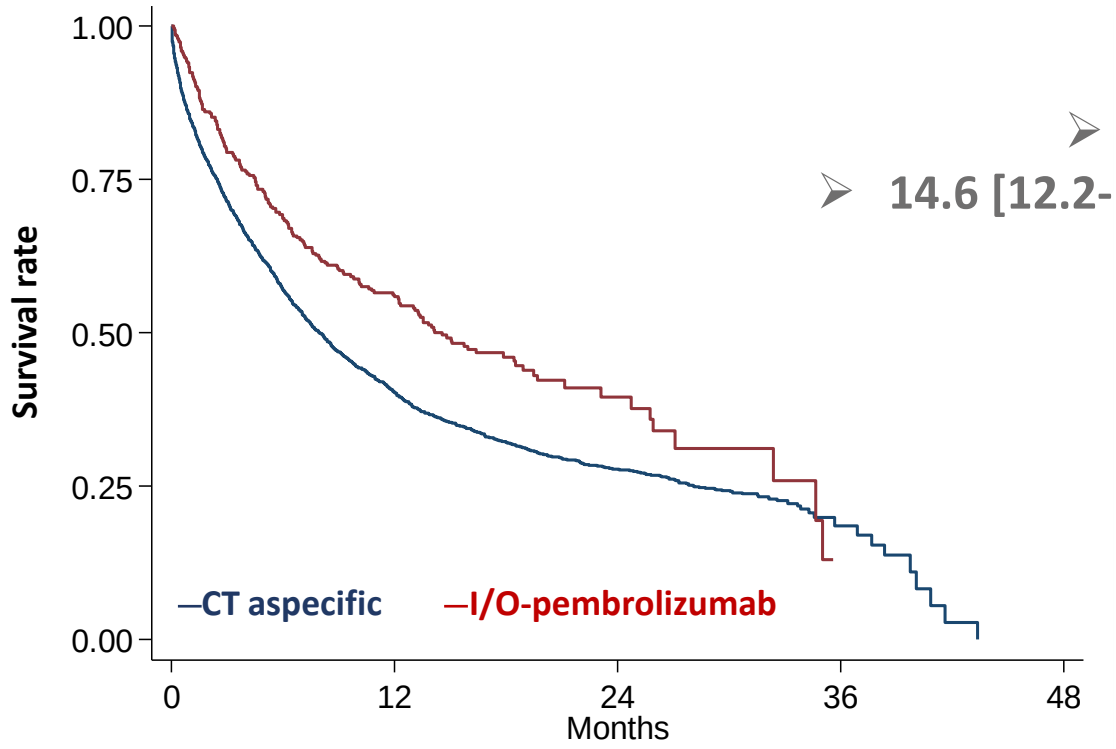
Patients with metastases were identified by the presence of at least one diagnosis of brain metastases (ICD-9-CM codes: 198.3X) bone metastases (ICD-9-CM codes 198.5X), liver metastases (ICD-9-CM codes: 197.7X)) metastasis of other respiratory organs (ICD-9-CM codes: 197.0X, 197.1X, 197.2X, 197.3X) metastasis of the adrenal gland (ICD-9-CM codes: 198.7X) metastasis of the peritoneum (codes ICD-9-CM: 197.6X), other metastases (ICD-9-CM codes: 197.XX, 198.XX not considered)

RESULTS-OVERALL SURVIVAL

KAPLAN-MEIER ANALYSIS OF OVERALL SURVIVAL IN met NSCLC PATIENTS IN FIRST LINE TREATMENT



Number at risk

CT aspecfic	3126	1100	389	12	0
I/O-pembrolizumab	316	163	25	0	0

The **median survival** [95% CI] was:

- **8.0 [7.4-8.6] months** for patients receiving **aspecific CT**
- **14.6 [12.2-18.9] months** for patients receiving **I/O-pembrolizumab**

NUMBER OF EVENTS

	Censored	%	Death	%
CT aspecific	975	31.2	2,151	68.8
I/O-pembrolizumab	140	44.3	176	55.7

The **death event** was observed in:

- **68.8%** of patients receiving **aspecific CT**
- **55.7%** of patients receiving **I/O-pembrolizumab**

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RESULTS-MULTIVARIATE PREDICTION OF MORTALITY
COX PROPORTION MODEL AND INDEPENDENT VARIABLES ASSOCIATED WITH MORTALITY RISK

A Cox proportional hazard model analysis was used as multivariate approach to analyse the **overall survival incidence** in both cohorts, adjusted for **age**, **sex**, **presence of metastasis**, **BRAF test**, and **pharmacological treatment**.

VARIABLES	HR	95% CI		P value
Age	1.024	1.019	1.028	<0.001
Sex (male)	1.170	1.068	1.281	0.001
Presence of metastasis				
Brain metastasis	1.718	1.549	1.906	<0.001
Bone metastasis	1.676	1.526	1.842	<0.001
Liver metastasis	1.549	1.389	1.728	<0.001
Respiratory tract metastasis	1.231	1.126	1.344	<0.001
Adrenal grands metastasis	1.369	1.177	1.593	<0.001
Peritoneum metastasis	1.404	1.100	1.792	0.006
Lymph node metastasis	0.957	0.878	1.043	0.315
Other sites metastasis	1.380	1.180	1.614	<0.001
BRAF test	0.972	0.925	1.023	0.276
Treatment with I/O-Pembrolizumab (vs CT aspecific*)	**0.796**	**0.681**	**0.930**	**0.004**

**The pharmacological treatment with chemotherapy was considered as reference.*

THE RISK OF DEATH WAS SIGNIFICANTLY **LOWER BY 20%** IN PATIENTS RECEIVING FIRST-LINE I/O VERSUS ASPECIFIC CT

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CONCLUSIONS
TAKE-HOME MESSAGE

1 The present analysis, conducted in a setting of **real clinical oncology practice**, highlighted a **higher survival** and a **reduced risk of death** in **met-NSCL patients** in the first line of treatment with I/O compared to aspecific CT.

2 Our findings suggest that **real-world data on cancer treatments and clinical outcomes**, captured in clinical practice, provides information that could complement and integrate the evidence generated by randomized controlled clinical trials [1,2].

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References:
[1] Di Maio M et al., Oncologist. 2020 May;25(5):e746-e752
[2] Karim S et al., J Clin Oncol 2019;37:1047–1050

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CONTACT INFORMATION:
Valentina Perrone
valentina.perrone@clicon.it

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