

Consistency of Metastatic Non-Small Cell Lung Cancer and Renal Cell Carcinoma Treatment Patterns Across Italian Regions

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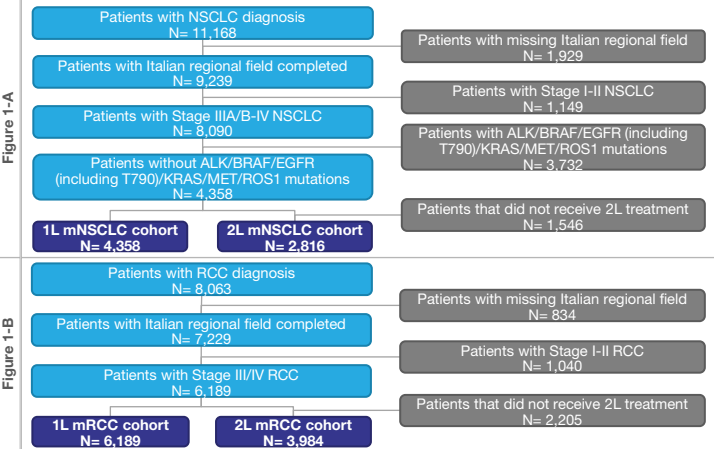
Background

- The therapeutic approach for advanced/metastatic non-small cell lung cancer (mNSCLC) has been recently revolutionized by immunotherapies (IOs), which demonstrated superior overall survival (OS) and sustained long-term benefits vs. chemotherapy, both in first-line (1L) and second-line (2L) settings.^{1,2}
- Similarly, advanced/metastatic renal cell carcinoma (mRCC) treatment landscape is under continuous evolution due to the recent survival benefit demonstrated by multiple IOs combinations (with anti-CTLA-4, TKI inhibitors or VEGFR inhibitors) vs. the current standard of care (tyrosine kinase inhibitors [TKIs]).³
- Upon EMA authorization, AIFA (supported by CTS and CPR) and the manufacturer starts the Italian HTA process to obtain reimbursed status at the national level. Once the national phase is completed (by decision publication in the Gazzetta Ufficiale—Italy's official journal), an oncology drug is not usually immediately available in every hospital. In fact, the drug approval process needs to undergo additional steps, which are region-specific, since the budgets are held by the Italian regions, and they are responsible for local provision of healthcare.⁴
- Recent studies have highlighted considerable delay in the average time from approval to first purchase of innovative cancer treatments in Italy (175 days), with significant differences across Italian regions (from 120.5 days in Lombardy (N) to 279.2 days in Basilicata (S)),⁴ which is likely manifested in regional treatment patterns.

Methods

- LiveTracker®, a large database of oncology and hematology patient charts across multiple oncology indications and countries was used to extract the granular Italian data needed for this analysis (see **Figure 1** and **Handout** for more details).
- For each patient, baseline characteristics, the type of systemic therapy received, the line of therapy (1L or 2L) and the Italian region and macro-region (North=N, Central=C, South=S, Islands=I) of care were extracted and analyzed. Details on how the therapies received were classified is provided in the **Handout**, along with further methods details.

Figure 1. Patient Disposition Diagram—NSCLC cohort and RCC cohort



Objective

- The aim of this study was to investigate within-country geographic differences across the 20 Italian regions, by examining treatment patterns in the first two lines of therapy (1L-2L) in mNSCLC and mRCC, between January 2019 and May 2021.
- Specifically, the objective was to quantify the proportion of patients receiving IOs, chemotherapies or targeted therapies in 1L-2L mNSCLC/ mRCC settings, within each Italian region and to compare across Italian regions.

Results

- The summary of baseline characteristics for both mNSCLC and mRCC is provided in the **Handout**.

mNSCLC Treatment Patterns

- In the mNSCLC cohort, the use of 1L IOs varied largely (**Figure 2** and **Table 2**), from 50.8% in Tuscany (Central [C]) to 15.1% in Calabria (South [S]) and 15.2% Molise (S). 1L chemotherapy was the dominant therapeutic approach across most regions, except Toscana (C) and Apulia (S).
- The use of 2L IOs (**Figure 3** and **Table 2**) was higher than chemotherapy across all regions, except Calabria (S), where a more limited IOs use (42.5%) was observed. Marked differences were found across regions, from >80% 2L IOs use in Apulia (S), Liguria (North [N]) and Molise (S) to <60% IOs use in Calabria (S) and Emilia-Romagna (N).
- Figure 2** and **Figure 3** help visualizing the lack of a distinct pattern of IOs use observable when comparing Italians macro-regions in 1L and 2L mNSCLC. In fact, the 1L IOs use (from 23.4% in the Islands to 35.5% in the North) and 2L IOs use (from 62.7% in the Islands to 70.8% in the Center) remained comparable across macro-regions.

mRCC Treatment Patterns

- In the mRCC 1L cohort (**Table 3**), the use of IOs remained very low (<10%) in 1L, except in Emilia-Romagna (N) and Valle D'Aosta (N), where the IOs use was 16.1% and 20.3%, respectively. TKIs represented the dominant 1L therapeutic approach across all regions, with the highest use (>95%) observed in Marche (C), Sicily (I), Friuli-Venezia Giulia (N) and Molise (S).

Figure 2. Proportion of patients receiving IOs as 1L treatment in mNSCLC



Results (Cont'd)

Table 2. Proportion of patients receiving IOs or chemotherapies in the 1L and 2L mNSCLC cohorts—stratified by Italian region

		mNSCLC - 1L Cohort			mNSCLC - 2L Cohort		
Macro-region	Region	Sample size	IOs	Chemotherapies	Sample size	IOs	Chemotherapies
Central	Lazio	417	29.3%	69.3%	283	73.5%	20.1%
Central	Marche	141	25.5%	73.8%	85	80.0%	18.8%
Central	Tuscany	120	50.8%	49.2%	68	50.0%	36.8%
Central	Umbria	6*	33.3%	66.7%	6*	50.0%	33.3%
Islands	Sardinia	2*	50.0%	50.0%	0*	0.0%	0.0%
Islands	Sicily	335	23.3%	54.9%	228	62.7%	14.9%
NE	Emilia-Romagna	457	45.1%	51.4%	279	51.3%	38.0%
NE	Friuli-Venezia Giulia	75	30.7%	69.3%	54	63.0%	31.5%
NE	Trentino-South Tyrol	11*	36.4%	63.6%	6*	50.0%	50.0%
NE	Veneto	325	38.2%	59.1%	210	67.1%	28.6%
NW	Liguria	76	30.3%	69.7%	51	100.0%	0.0%
NW	Lombardy	1119	32.6%	61.1%	737	69.1%	22.0%
NW	Piedmont	268	31.3%	66.0%	158	73.4%	15.2%
NW	Aosta Valley	17*	35.3%	52.9%	12*	75.0%	25.0%
South	Basilicata	216	25.5%	71.8%	150	74.0%	20.0%
South	Calabria	192	15.1%	78.6%	127	42.5%	56.7%
South	Campania	393	28.0%	65.9%	240	77.5%	15.4%
South	Molise	33	15.2%	84.8%	20	95.0%	5.0%
South	Apulia	80	47.5%	41.3%	50	86.0%	14.0%

Data for South | Abruzzo were not available; NE= North East, NW= North West
*Regions with sample size below 20 should not be considered for results discussion and to draw conclusions. However, these are included in the table for completeness.

Figure 3. Proportion of patients receiving IOs as 2L treatment in mNSCLC



- The majority of 2L mRCC patients (**Table 3**) were on IOs except in Calabria(S) and Basilicata(S), where TKIs remained dominant with 57.3% and 58.1%, respectively. The use of 2L IOs was greatest at 83.7% in Marche (C), with Apulia (S) and Veneto (N) also showing large 2L IOs use (77.5% and 69.5%).
- Similar to the mNSCLC analysis, a lack of a distinct pattern of IOs use was observable when comparing Italians macro-regions in 1L mRCC, which spanned from 6.2% in the South to 9.4% in the North. A trend of higher 2L IOs use was observed in the North and Center macro-region (60.5% and 65.8%) vs. the South macro-region (41.3%).

Table 3. Proportion of patients receiving IOs or TKIs in the 1L and 2L mRCC cohorts—stratified by Italian region

		mRCC - 1L Cohort			mRCC - 2L Cohort		
Macro-region	Region	Sample size	IOs	TKIs	Sample size	IOs	TKIs
Central	Lazio	542	9.0%	84.9%	354	60.7%	31.1%
Central	Marche	159	1.9%	98.1%	98	83.7%	16.3%
Central	Tuscany	120	4.2%	85.8%	67	65.7%	23.9%
Central	Umbria	2*	0.0%	100.0%	2*	100.0%	0.0%
Islands	Sardinia	487	2.1%	96.5%	326	65.0%	31.3%
Islands	Sicily	527	16.1%	78.6%	333	62.2%	35.4%
NE	Emilia-Romagna	123	4.9%	95.1%	78	60.3%	39.7%
NE	Friuli-Venezia Giulia	7*	0.0%	100.0%	3*	100.0%	0.0%
NE	Trentino-South Tyrol	451	6.0%	93.1%	269	69.5%	23.8%
NE	Veneto	1937	8.4%	76.1%	1287	58.8%	32.0%
NW	Liguria	426	8.7%	89.9%	283	59.0%	38.2%
NW	Lombardy	69	20.3%	79.7%	48	52.1%	47.9%
NW	Piedmont	308	3.9%	92.9%	199	41.2%	57.3%
NW	Aosta Valley	314	3.5%	60.5%	210	15.7%	58.1%
South	Basilicata	591	9.6%	88.0%	337	50.4%	38.0%
South	Calabria	76	0.0%	100.0%	50	58.0%	42.0%
South	Campania	48	6.3%	91.7%	40	77.5%	22.5%
South	Molise	542	9.0%	84.9%	354	60.7%	31.1%
South	Apulia	159	1.9%	98.1%	98	83.7%	16.3%

Data for South | Abruzzo were not available; NE= North East, NW= North West, TKIs= Tyrosine kinase inhibitors
*Regions with sample size below 20 should not be considered for results discussion and to draw conclusions. However, these are included in the table for completeness.

Discussion & Conclusions

- Contemporary and granular real-world evidence on mNSCLC/mRCC treatment landscape in Italy shows that 1L-2L systemic therapy treatment patterns in mNSCLC and mRCC remain heterogeneous across regions, and do not align with macro-regions, but potentially with centers of excellence.
- Region-specific delays in novel therapies listing might also be one of the drivers of novel therapies uptake, since some of the regions with largest IOs use in our analysis (1L-2L mNSCLC: Apulia; mRCC: 1L - Aosta Valley and 2L - Apulia) were also the regions with the lowest time from AIFA approval to first purchase (i.e. implying faster regional listing) in a recent analysis by Prada and colleagues.⁴
 - However, it is likely not the only driver since high IOs use in mNSCLC (1L: Tuscany, Emilia-Romagna ; 2L: Marche, Molise) and mRCC (1L: Emilia-Romagna; 2L: Marche, Veneto) was also observed in regions with relatively long time from AIFA approval to first purchase, according to Prada et al.⁴
 - Selection bias of clinicians self-selecting from various hospitals to contribute to the chart reviews could also explain some of the differences.
- Further interviews can shed light on this rich set of information that the administrative data reveal along with continued examination of treatment trends using LiveTracker® data across the Italian regions.

References

- Ascierto PA, et al. *J Transl Med.* 2021;19(1):13.
- Planchard D, et al. *Ann Oncol.* 2020;29(Suppl 4):iv192-iv237.
- Powles T, Albiges L, Bex A, et al. ESMO Clinical Practice Guideline update on the use of immunotherapy in early stage and advanced renal cell carcinoma. *Ann Oncol.*
- Prada M, Ruggeri M, Sansone C, et al. Timeline of Authorization and Reimbursement for Oncology Drugs in Italy in the Last 3 Years. *Medicine Access @ Point of Care.* 2017;1:maapoc.0000007