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Characteristics and treatment patterns of patients with advanced or metastatic non-small cell lung cancer managed with first-line immuno-oncology strategies in Greece:

Interim results of the real-world multicenter prospective study (IO-HORIZON)

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Background

The advent of immunotherapies in routine clinical practice has drastically altered the treatment paradigm for patients with advanced/metastatic non-small cell lung cancer (NSCLC) lacking a targetable molecular driver.[1]

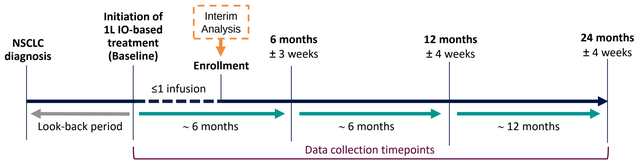
- At the time of study design and up to 2020, pembrolizumab, which targets the programmed cell death-1 (PD-1) receptor, was the only immune-oncology (IO) agent approved by the European Medicines Agency and recommended by the European Society for Medical Oncology in the first-line (1L) setting of metastatic NSCLC.[2,3]
- Since then, other IO agents have been approved in this setting including also anti-programmed death-ligand 1 (PD-L1) agents.[4,5]

In light of this quickly evolving landscape, and taking into consideration the absence of a nationwide NSCLC patient registry, the present study aims to characterize the profile of patients with advanced or metastatic NSCLC managed with 1L IO treatments, to capture treatment utilization patterns and to measure disease-related resource consumption in routine clinical settings of Greece.

Methods

- **IO-HORIZON** is an **ongoing**, non-interventional, multicenter, prospective cohort study of patients with locally advanced or metastatic NSCLC regardless of histological subtype with no Epidermal Growth Factor Receptor (EGFR) mutations or Anaplastic Lymphoma Kinase (ALK) translocations, who had been prescribed 1L treatment with commercially available IO agent(s) (anti-PD-1 or anti-PD-L1 agents).
- Data are collected during routine clinic visits. The study design, eligibility criteria, and objectives are shown in **Figure 1**.
- We present herein results of the protocol-planned **interim** baseline cross-sectional analysis after **patient accrual completion** primarily aiming at gaining insight into the clinical profile and characteristics of advanced/metastatic NSCLC patients initiating 1L IO-based therapy in routine care.

Figure 1. IO-HORIZON study design



Inclusion criteria

1. Male or female patient ≥18 years at the time of informed consent.
2. Diagnosis of locally advanced or metastatic (stage IIIb-IV) NSCLC, of any histology.
3. Prescription of locally approved commercially available IO-based treatment (anti-PD-1 or anti-PD-L1 agent) as per the agent's SmPC prior to signed informed consent and, if treatment had started, no more than one infusion had been administered.
4. The decision to prescribe IO-based treatment had already been taken prior to patient's enrollment in the study and is clearly separated from the physician's decision to include the patient in the current study.

Exclusion criteria

1. Current primary diagnosis of cancer other than NSCLC that requires any treatment.
2. Receipt of any prior systemic therapy for advanced/metastatic disease.
3. EGFR-sensitizing mutation and/or ALK translocation.
4. Participation in any interventional clinical trial.

Primary objective

- To characterize the profile of patients routinely managed with IO treatments (either as monotherapy or as combination regimens) in the 1L setting of advanced/metastatic NSCLC, overall and by IO treatment option.

Secondary objectives

- To determine factors among baseline patient and disease characteristics potentially affecting 1L IO treatment choices.
- To capture 1L immunotherapy utilization patterns by IO treatment option.
- To estimate the time on 1L IO treatment, overall and by IO treatment option.
- To measure the burden of disease management on the healthcare and non-healthcare resource utilization (HCRU), overall and by IO treatment option.
- To examine the relationship between 1L IO treatment options and inpatient and outpatient HCRU rates.

Statistical considerations

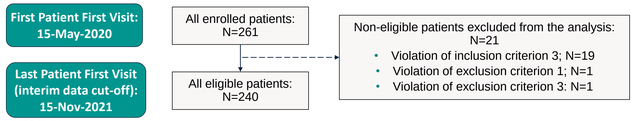
- The normality of distribution of continuous variables was examined with the Shapiro-Wilk test.
- Summary statistics of continuous variables are presented as mean (SD) when data follow a normal distribution; otherwise, the median (interquartile range; IQR) is presented. For variables not following a normal distribution in at least one of the study (sub)populations, a uniform presentation of median (IQR) was applied.
- Statistical analyses were performed using SAS® software (version 9.4)

Results

Patient disposition

A total of **240 eligible NSCLC patients** were enrolled by 17 public (N=10) or private (N=7) sector hospital centers/clinics in Greece specializing in lung cancer (**Figure 2**).

Figure 2. IO-HORIZON milestones and patient disposition

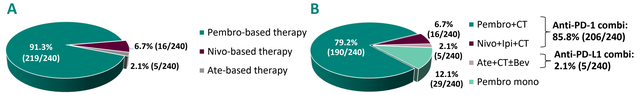


N, number of patients.

Immunotherapy patterns

The majority of patients (87.9%; 211/240) received **anti-PD(L)1 combination therapy**. Detailed frequencies of 1L IO based treatment patterns are presented in **Figure 3**.

Figure 3. 1L IO-based treatments



A. At an IO agent level.
B. At an IO-based regimen level.

Ate, atezolizumab; Bev, bevacizumab; combi, combination (therapy); CT, chemotherapy; IO, immuno-oncology; Ipi, ipilimumab; mono, monotherapy; Nivo, nivolumab; PD-1: Programmed Cell Death-1; PD-L1, Programmed-Death Ligand 1; pembro, pembrolizumab.

Patient and disease characteristics

All patients were Caucasian. Key patient characteristics at 1L-IO based treatment initiation are presented in **Table 1**.

Table 1. Key patient characteristics at 1L IO treatment initiation

		Monotherapy	Combination therapy			
	Overall (N=240)	Pembro (N=29)	Total Anti-PD-(L)1 (N=211)	Pembro+CT (N=190)	Nivo+Ipi+CT (N=16)	Ate+Bev±CT (N=5)
Age, years, median (IQR)	69.0 (62.2-75.2)	75.5 (63.2-81.3)	68.7 (62.2-74.7)	68.9 (62.4-74.8)	69.2 (60.7-74.7)	62.1 (51.0-62.2)
Age ≥70 years, % (n/N)	45.0 (108/240)	58.6 (17/29)	43.1 (91/211)	43.2 (82/190)	50.0 (8/16)	20.0 (1/5)
Male, % (n/N)	75.4 (181/240)	65.5 (19/29)	76.8 (162/211)	76.8 (146/190)	81.3 (13/16)	60.0 (3/5)
Urban residence, % (n/N)	73.3 (176/240)	69.0 (20/29)	73.9 (156/211)	75.8 (144/190)	50.0 (8/16)	80.0 (4/5)
Former smokers, % (n/N)	64.2 (154/240)	55.2 (16/29)	65.4 (138/211)	65.3 (124/190)	56.3 (9/16)	100.0 (5/5)
Current smokers, % (n/N)	27.1 (65/240)	20.7 (6/29)	28.0 (59/211)	27.9 (53/190)	37.5 (6/16)	.
Pack-years[a], median (IQR)	50.0 (35.0-80.0)	56.5 (30.0-80.0)	50.0 (35.0-80.0)	50.0 (35.0-80.0)	52.5 (31.3-74.0)	45.0 (40.0-50.0)
BMI, median (IQR)	25.2 (23.0-28.3)	25.7 (22.9-26.4)	25.2 (23.0-28.7)[b]	25.2 (23.0-28.7)[b]	24.7 (24.1-27.7)	25.5 (25.2-25.8)
ECOG Performance status (PS)						
PS 0, % (n/N)	62.5 (150/240)	51.7 (15/29)	64.0 (135/211)	63.2 (120/190)	68.8 (11/16)	80.0 (4/5)
PS 1, % (n/N)	31.3 (75/240)	31.0 (9/29)	31.3 (66/211)	31.6 (60/190)	31.3 (5/16)	20.0 (1/5)
PS 2, % (n/N)	6.3 (15/240)	17.2 (5/29)	4.7 (10/211)	5.3 (10/190)	.	.
Comorbidity[c], % (n/N)	70.8 (170/240)	62.1 (18/29)	72.0 (152/211)	74.2 (141/190)	50.0 (8/16)	60.0 (3/5)
≥2 comorbidities	48.3 (116/240)	48.3 (14/29)	48.3 (102/211)	50.5 (96/190)	18.8 (3/16)	60.0 (3/5)

[a]For ever smokers (i.e., current and former); [b]BMI was unknown for one patient; [c]Clinically significant.
1L, first-line; Ate, atezolizumab; Bev, bevacizumab; BMI, body mass index; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; IO, immuno-oncology; Ipi, ipilimumab; IQR, interquartile range; n, number of patients; N, number of patients with available data; Nivo, nivolumab; PD-1: Programmed Cell Death-1; PD-L1, Programmed-Death Ligand 1; pembro, pembrolizumab.

Patient and disease characteristics (continued)

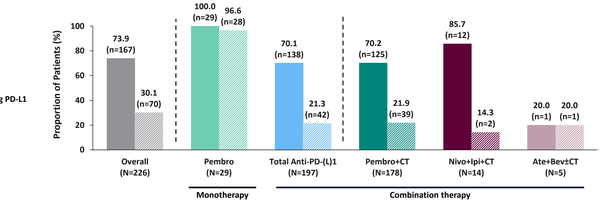
Comorbidities

- The median (IQR) number of past or ongoing clinically significant medical conditions/surgical procedures was 3.0 (2.0-4.0).
- Clinically significant comorbidities at 1L IO treatment initiation (in >10% of patients) included **hypertension** (36.3%; 87/240), **dyslipidaemia** (24.2%; 58/240), **diabetes mellitus** (19.2%; 46/240) and **chronic obstructive pulmonary disease** (14.2%; 34/240).
- History of other past **primary malignancy** was reported for 8.8% (21/240) of the patients.

PD-L1 expression

- Of the patients, 94.1% (226/240) had undergone 234 PD-L1 testings in the context of NSCLC; results are presented in **Figure 4**.
- The most common type of specimen tested was **small biopsy** for 69.7% (163/234) of the testings, followed by **cytology** and **surgical resection specimen** in 15.4% (36/234) and 15.0% (35/234) of the testings, respectively.
- The most common PD-L1 assays used were **PD-L1 IHC 22C3 pharmDx** and **VENTANA PD-L1 SP263** for 57.3% (133/232) and 37.9% (88/232) of the testings with available data, respectively.

Figure 4. PD-L1 expression rate based on most recent assessment before 1L IO treatment initiation among tested patients

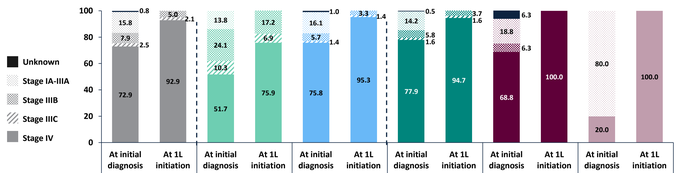


1LT, first-line treatment; Ate, atezolizumab; Bev, bevacizumab; CT, chemotherapy; Ipi, ipilimumab; n, number of patients; N, number of patients with available data; Nivo, nivolumab; PD-1: Programmed Cell Death-1; PD-L1, Programmed-Death Ligand 1; pembro, pembrolizumab; TPS: tumor proportion score.

NSCLC characteristics

- Key NSCLC characteristics are presented in **Figure 5**.
- Disease staging at initial diagnosis and 1L treatment initiation was based on UICC TNM 8th Edition criteria in the majority of cases (>85%).

Figure 5. NSCLC stage and disease characteristics prior to initiation of 1L IO treatment

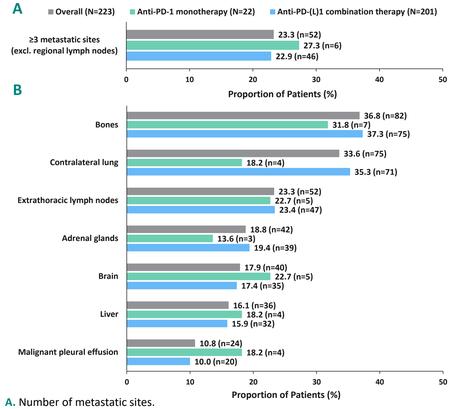


	Overall (N=240)	Pembro (N=29)	Total Anti-PD-(L)1 (N=211)	Pembro+CT (N=190)	Nivo+Ipi+CT (N=16)	Ate+Bev±CT (N=5)
Adenocarcinoma, % (n/N)	68.8 (165/240)	62.1 (18/29)	69.7 (147/211)	72.1 (137/190)	31.3 (5/16)	100.0 (5/5)
Pure SCC, % (n/N)	23.3 (56/240)	24.1 (7/29)	23.2 (49/211)	20.5 (39/190)	62.5 (10/16)	.
De novo Stage IV[a], % (n/N)	78.5 (175/223)	68.2 (15/22)	79.6 (160/201)	82.2 (148/180)	68.8 (11/16)	20.0 (1/5)
Months from:	n median (IQR)	n median (IQR)	n median (IQR)	n median (IQR)	n median (IQR)	n median (IQR)
Initial to A/M diagnosis[b]	38 16.3 (9.3-26.6)	4 12.7 (7.1-21.5)	34 16.3 (9.6-27.2)	27 16.3 (9.6-32.6)	3 12.9 (4.2-36.3)	4 14.0 (9.7-20.0)
A/M diagnosis to 1LT	240 2.0 (1.5-2.6)	29 1.6 (1.3-2.4)	211 2.0 (1.5-2.7)	190 2.0 (1.5-2.6)	16 2.0 (1.4-3.0)	5 3.3 (1.4-3.4)

Among patients with stage IV disease at baseline in the six distinct subgroups, 9,3,6,5,1 and 0 patients had de novo stage IIIB or stage IIIC disease.
[a]Among patients with Stage IV NSCLC at 1L initiation; [b]Among patients initially diagnosed at an earlier disease stage (i.e., excluding de novo locally advanced or metastatic diagnoses).
1L: first-line; 1LT, 1L treatment; A/M, advanced/metastatic; Ate, atezolizumab; Bev, bevacizumab; CT, chemotherapy; IO, immuno-oncology; IQR, interquartile range; Ipi, ipilimumab; NSCLC, non-small cell lung cancer; n, number of patients; N, number of patients with available data; Nivo, nivolumab; PD-1: Programmed Cell Death-1; PD-L1, Programmed-Death Ligand 1; pembro, pembrolizumab; SCC, squamous cell carcinoma.

- Patients with *de novo* metastatic disease and available data (N=168), had a median (IQR) of 3.0 (1.0-5.0) metastatic lesions (excl. regional lymph nodes) at initial NSCLC diagnosis.
- Information on metastatic sites among Stage IV NSCLC patients is provided in **Figure 6**.

Figure 6. Metastases at 1L IO treatment initiation in patients with metastatic NSCLC



A. Number of metastatic sites.
B. Localization of metastatic lesions.

1L: first-line; IO, immuno-oncology; n, number of patients; N, number of patients with available data; NSCLC, non-small cell lung cancer; PD-1: Programmed Cell Death-1; PD-L1, Programmed-Death Ligand 1.

Limitations

- Limitations, attributable to study observational design, involve patient selection and information bias
  - ✓ Patient selecton bias was mitigated through consecutive sampling
  - ✓ Data missingness rate was low (<10% in key variables of interest)
- The small size of IO treatment subgroups of interest, adversely affects the precision of the estimates.

Conclusions

- These results yield novel RWE on the profile and 1L IO treatment patterns of advanced/metastatic NSCLC patients in Greece. Such data help to better understand disease and therapy approaches so as to design informed health policy strategies.

Disclosures

- Linardou H. has served as lecturer and/or consultant for Amgen, AstraZeneca, Bristol Myers Squibb, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, Takeda. Charpidou A. has served as lecturer and/or consultant for AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, MSD, Pfizer, Roche. Koumarianou A. has served as lecturer and/or consultant or has received educational grants from Bristol Myers Squibb, Genesis Pharma, Ipsen, Merck KGaA, MSD, Novartis, Pfizer, Roche. Mountzios I. has served as lecturer and/or consultant for Amgen, AstraZeneca, Bristol Myers Squibb, GlaxoSmithKline, MSD, Novartis, Pfizer, Roche, Sanofi, Takeda. Kosmidis P. has no conflict of interest to declare. Christodoulou C. has served as lecturer and/or consultant for AstraZeneca, Bristol Myers Squibb, Genesis Pharma, MSD, Novartis, Pfizer, Roche, Sanofi. Mavroudis D. has served as consultant for MSD. Christopoulou A. has served as lecturer and/or consultant for Astellas, AstraZeneca, Bristol Myers Squibb, GlaxoSmithKline, Ipsen, Janssen, Merck KGaA, MSD, Novartis, Pfizer, Roche, Sanofi. Korantzis I. has served as lecturer and/or consultant for Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Merck, KGaA, MSD, Novartis, Pfizer, Roche, Sandoz, Sanofi. Baka S. has served as lecturer and/or consultant for AstraZeneca, Boehringer Ingelheim Bristol Myers Squibb, Genesis Pharma, Lilly, MSD, Novartis, Roche, Takeda. Vaslamatzis M. has no conflict of interest to declare. Athanasiadis I. has served as lecturer and/or consultant for Amgen, AstraZeneca, Bristol Myers Squibb, GlaxoSmithKline, Ipsen, Lilly, MSD, Novartis, Pfizer, Roche, Servier. Koutras A. has served as lecturer and/or consultant for AstraZeneca, Genesis Pharma, GlaxoSmithKline, MSD, Novartis, Roche. Mauri D. has served as lecturer and/or consultant for Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, GlaxoSmithKline, Janssen, MSD, Novartis, Roche, Takeda, Sanofi. Kotsakis A. has received research grants and has served as consultant for AstraZeneca, Bristol Myers Squibb, MSD, Roche. Ziogas D.C. has served as lecturer for MSD. Desiniotis A. is employee of MSD LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. Dimitriadis I. is employee of MSD LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. Syrigos K.N. has served as lecturer and/or consultant for AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda.
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References

1. Mamdani H, et al. *Front Immunol.* 2022;13:823618.
2. Planchard D, et al. *Ann Oncol.* 2018;29(Suppl 4):iv192-iv237. Update at: https://www.esmo.org/content/download/347819/6034778/1/ESMO-CPG-mNSCLC-15SEPT2020.pdf.
3. KEYTRUDA®. Summary of Product Characteristics.
4. TECENTRIQ®. Summary of Product Characteristics.
5. OPDIVO®. Summary of Product Characteristics.

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