25P Association between the lung immune prognostic index (LIPI) and durvalumab consolidation outcomes in patients with locally advanced non-small cell lung cancer (NSCLC)

M. Riudavets Melia[1], E. Auclin[2], F. Aboubakar[3], S. Ponce Aix[4], A. Dal Maso[5], V. Bluthgen[6], X. Mielgo[7], E. Mussat[2], R. Reyes[8], J. Benítez[9], L. Lupinacci[10], B. Duchemann[11], A. de Giglio[12], J. Bautista[13], C. Audigier-Valette[14], M. Scheffler[15], M. Campayo[9], B. Besse[1], D. Planchard[1], L. Mezquita[8]

[1]*Medical Oncology Department, Gustave Roussy Cancer Campus, Villejuif, France;* [2]*Medical Oncology Department, Hôpital Européen George Pompidou, Paris, France;* [3]*Medical Oncology Department, Cliniques Universitaires Saint-Luc, Brussels, Belgium;* [4]*Medical Oncology Department, Hospital 12 de Octubre, Madrid, Spain;* [5]*Medical Oncology Department, Istituto Oncologico Veneto IOV - IRCCS, Padua, Italy;* [6]*Medical Oncology Department, Hospital Aleman, Buenos Aires, Argentina;* [7]*Medical Oncology Department, Hospital Fundación Alcorcón, Madrid, Spain;* [8]*Medical Oncology Department, Hospital Clinic i Provincial de Barcelona; IDIBAPS, Barcelona, Spain;* [9]*Medical Oncology Department, Hospital Mútua de Terrassa, Terrassa, Spain;* [10]*Medical Oncology Department, Hospital Italiano, Buenos Aires, Argentina;* [11]*Medical Oncology Department, Hôpital Avicenne, Bobigny, France;* [12]*Medical Oncology Department, Sant'Orsola-Malpighi Ospedale, Bologna, Italy;* [13]*Medical Oncology Department, Centro de Educación Médica e Investigaciones Clínicas (CEMIC), Buenos Aires, Argentina;* [14]*Medical Oncology Department, Centre Hospitalier Toulon Sainte-Mousse, Toulon, France;* [15]*Medical Oncology Department, University Hospital of Cologne, Cologne, Germany*

Background: The LIPI, based on pretreatment derived neutrophils/[leukocytes-neutrophils] ratio (dNLR) >3 and lactate dehydrogenase (LDH) >upper limit of normal (ULN), is associated with immune checkpoint inhibitors (ICI) outcomes in advanced non-small cell lung cancer (NSCLC). We aimed to assess if baseline LIPI correlates with durvalumab efficacy after chemoradiotherapy (ChRT) in the locally advanced setting.

Methods: Multicentre retrospective study with 26 centres from Europe/America, including 330 patients with locally advanced NSCLC treated durvalumab after ChRT between 4.2015 and 12.2020, and 65 patients treated with ChRT only. Clinical and biological data before treatment were collected. LIPI was calculated characterizing 3 groups: good (dNLR≤3+LDH≤ULN), intermediate (dNLR>3/LDH>ULN) and poor (dNLR>3+LDH>ULN). Our primary endpoint was overall survival (OS). Secondary endpoints were progression-free survival (PFS) and response.

Results: In the immuno-cohort, median age was 67 years [38-85], 70% of patients were male, 95% smokers, and 98% had a performance status of 0-1; 60% had non-squamous histology and PD-L1 expression was <1% in 16% (not available in 34 patients). Radiotherapy was delivered concomitantly in 81% of patients. LIPI was evaluable in 216 patients: 66% were considered good, 31% intermediate and 3% as poor LIPI groups. With a median follow-up of 19 mo. [95%CI, 17-21], LIPI was significantly correlated with median OS and a trend between response and LIPI groups was observed (Table).

The pooled intermediate/poor LIPI group was associated with a shorter OS (HR 1.97; P=0.03) and progressive disease (OR 2.68; P=0.047). Survivals and response were non-significant in the control-cohort.

Conclusions: Pretreatment LIPI was correlated with outcomes in patients with locally advanced NSCLC treated with durvalumab consolidation, but not with ChRT only, providing further evidence of its prognostic and potential predictive role of ICI benefit in lung cancer.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: B. Besse: Financial Interests, Institutional, Sponsor/Funding: AbbVie; Financial Interests, Institutional, Sponsor/Funding: Amgen; Financial Interests, Institutional, Sponsor/Funding: AstraZeneca; Financial Interests, Institutional, Sponsor/Funding: Biogen; Financial Interests, Institutional, Sponsor/Funding: Blueprint Medicine; Financial Interests, Institutional, Sponsor/Funding: Bristol Myers Squibb; Financial Interests, Institutional, Sponsor/Funding: Celgene; Financial Interests, Institutional, Sponsor/Funding: Eli Lilly; Financial Interests, Institutional, Sponsor/Funding: GlaxoSmithKline; Financial Interests, Institutional, Sponsor/Funding: Ignyta; Financial Interests, Institutional, Sponsor/Funding: IPSEN; Financial Interests, Institutional, Sponsor/Funding: Merck KGaA; Financial Interests, Institutional, Sponsor/Funding: MSD; Financial Interests, Institutional, Sponsor/Funding: Nektar; Financial Interests, Institutional, Sponsor/Funding: Onxeo; Financial Interests, Institutional, Sponsor/Funding: Pfizer; Financial Interests, Institutional, Sponsor/Funding: Pharma Mar; Financial Interests, Institutional, Sponsor/Funding: Sanofi; Financial Interests, Institutional, Sponsor/Funding: Spectrum Pharmaceuticals; Financial Interests, Institutional, Sponsor/Funding: Takeda; Financial Interests, Institutional, Sponsor/Funding: Tiziana Pharma. D. Planchard: Financial Interests, Personal and Institutional, Advisory Role: AstraZeneca; Financial Interests, Personal and Institutional, Advisory Role: Bristol Myers Squibb; Financial Interests, Personal and Institutional, Advisory Role: Boehringer Ingelheim; Financial Interests, Personal and Institutional, Advisory Role: Celgene; Financial Interests, Personal and Institutional, Advisory Role: Daiichi Sankyo; Financial Interests, Personal and Institutional, Advisory Role: Eli Lilly; Financial Interests, Personal and Institutional, Advisory Role: Merck; Financial Interests, Personal and Institutional, Advisory Role: Novartis; Financial Interests, Personal and Institutional, Advisory Role: Pfizer; Financial Interests, Personal and Institutional, Advisory Role: prIME Oncology; Financial Interests, Personal and Institutional, Advisory Role: Peer CME; Financial Interests, Personal and Institutional, Advisory Role: Roche; Financial Interests, Institutional, Sponsor/Funding: Medimmune; Financial Interests, Institutional, Sponsor/Funding: Sanofi-Aventis; Financial Interests, Institutional, Sponsor/Funding: Taiho Pharma; Financial Interests, Institutional, Sponsor/Funding: Novocure. L. Mezquita: Financial Interests, Personal, Research Grant: Bristol Myers Squibb; Financial Interests, Personal, Research Grant: Boehringer Ingelheim; Financial Interests, Personal, Research Grant: Amgen; Financial Interests, Personal, Research Grant: Stilla; Financial Interests, Personal, Research Grant: Inivata; Financial Interests, Institutional, Advisory Board: Roche Diagnostics; Financial Interests, Institutional, Advisory Board: Takeda; Financial Interests, Personal, Invited Speaker: Tecnofarma; Financial Interests, Personal, Other: Roche; Financial Interests, Personal, Other: AstraZeneca. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.10.041

26P Genome-wide copy number variation of circulating cell-free DNA as a biomarker in head and neck cancer patients treated with immunotherapy

Y. Zhu[1], S. Yang[1], L. Jiang[2], X. Wang[2], X. He[1]

[1]*Department of Medical Oncology, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, National Cancer Center/ National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China;* [2]*State Key Laboratory of Molecular Oncology, National Cancer Center/ National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Advanced head and neck cancer (AHNC) is a type of malignancy with a poor prognosis. Recently, many clinical studies have shown that immunotherapy can improve the prognosis of AHNC. It is difficult for AHNC patients to obtain tissue specimens due to advanced disease. Liquid biopsy based on cell-free DNA (cfDNA) has shown good results in monitoring treatment outcomes. But so far, the research of cfDNA for AHNC in immunotherapy are few.

Methods: Baseline blood samples of 26 AHNC patients before immunotherapy and 50 healthy control blood samples were collected. Of these, 15 patients were dynamically monitored during treatment. Shallow whole genome sequencing (sWGS) of cfDNA was used to identify copy number variations (CNV), and a metric was developed—IS score—to describe the genome instability. The primary aim of this study was the association between biomarker with treatment efficacy including disease control rate (DCR) and progression-free survival (PFS) in these patients.

Results: CNV reproducibility analysis revealed that chromosomal arm significant alterations included copy number losses (CNL) in 21p、17p、22q、19q and 3p, and gains of 21p and 8q (q<0.05). The most frequent CNVs were losses in 17p (harbouring the TP53 and NCOR1 genes) and 22q (harbouring the NF2 and EP300 genes). Compared with the baseline plasma cfDNA sequencing results, patients with progressive disease (PD) after immunotherapy have observed more obvious genomic instability events. The CNL in 17p/22q (7.4 vs. 17.3 months; P=0.0170) and the IS-score-high group (7.4 vs. 19.9 months; P=0.0026) had poorer PFS. The median IS-score of patients with PD was significantly higher than those with disease control (P=0.0089), however, there was no significant difference in cfDNA concentration between the two groups. The IS-score was not significantly correlated with the cfDNA concentration (P=0.48). In the multivariable analyses, the IS-score remained an independent prognostic factor for PFS (P=0.037).

Conclusions: IS-score is a potential biomarker in predicting the prognosis of AHNC patients receiving immunotherapy, help identify high-risk patients, and guide clinical decision-making.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.10.042

Table: 25P

	Overall (n=330)	LIPI good (N=142)	LIPI intermediate (N=67)	LIPI poor (N=7)	P value
OS, mo. (95% CI)	47.0 (30.8-NR)	not reached (NR-NR)	47.0 (29.4-NR)	18.1 (8.5-NR)	0.03
PFS, mo. (95% CI)	18.0 (14.0-24.3)	19.0 (14.4-NR)	12.9 (7.9-NR)	7.5 (5.0-NR)	0.20
ORR, %	44	45	41	0	0.05
DCR, %	87	90	78	100	0.06