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Durvalumab consolidation in patients with stage III non-resectable NSCLC with driver genomic alterations

M. Riudavets Melia¹, E. Auclin², M.A. Mosteiro Lamas³, N. Dempsey⁴, M. Majem⁵, R. Lobefaro⁶, R. Lopez Castro⁷, J. Bosch Barrera⁸, S. Pilotto⁹, E. Escalera Martín¹⁰, M. Tagliamento¹¹, J. Mosquera Martinez¹², G. Zalcman¹³, E. Nadal³, G. Lopes⁴, D. Signorelli⁶, M.R. Garcia Campelo¹², B. Besse¹, D. Planchard¹, L. Mezquita¹⁴

¹ Medical Oncology Department, Gustave Roussy Cancer Campus, Villejuif, France, ² Medical Oncology Department, Hôpital Européen Georges Pompidou, Paris, France, ³ Medical Oncology Department, ICO - Institut Català d'Oncologia l'Hospitalet (Hospital Duran i Reynals), L'Hospitalet de Llobregat, Spain, ⁴ Medical Oncology Department, Sylvester Comprehensive Cancer Center - University of Miami, Miami, FL, USA, ⁵ Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, ⁶ Medical Oncology Department, Istituto Nazionale dei Tumori di Milano - Fondazione IRCCS, Milan, Italy, ⁷ Medical Oncology Department, Hospital Clínico Universitario de Valladolid, Valladolid, Spain, ⁸ Medical Oncology Department, ICO - Institut Català d'Oncologia Girona (Hospital Universitari Josep Trueta), L'Hospitalet de Llobregat, Spain, ⁹ Medical Oncology Department, University and Hospital Trust of Verona, Verona, Italy, ¹⁰ Medical Oncology Department, Hospital Clínico de Salamanca, Salamanca, Spain, ¹¹ Medical Oncology Department, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, ¹² Medical Oncology Department, CHUAC - Complejo Hospitalario Universitario A Coruña, A Coruña, Spain, ¹³ Medical Oncology Department, Hôpital Bichat Claude Bernard, Paris, France ¹⁴ Medical Oncology Department, Hospital Clínic i Provincial de Barcelona, Barcelona, Spain

Background

Durvalumab is the standard-of-care as consolidation therapy after chemo-radiation (ChRT) in stage III non-resectable non-small cell lung cancer (NSCLC). Its activity across NSCLC patients (pts) with genomic alterations (GA) is poorly characterized. We aimed to assess durvalumab outcomes in the context of oncogenic addition.

Methods

Retrospective study of pts with stage III non-resectable NSCLC treated with durvalumab after ChRT between Apr/15 and Oct/20 at 25 centres from Europe and United States. Clinical and biological data were collected; driver GA (dGA) included *EGFR*/all-*BRAF*/all-*KRAS* mutations (m) and *ALK*/*ROS1* rearrangements (r). Radiological response was assessed according to RECIST v1.1 or investigator's criteria. We evaluated progression-free survival (PFS) and overall survival (OS) based on dGA.

Results

Out of 323 pts included, 43 had one dGA: *KRAS*m (26; n=8 G12C), *EGFR*m (8; n=6 del19/ex21), *BRAF*m (5; n=4 V600E) and *ALK*r (4). Median age was 66 [39-84], gender ratio 1:1, with 98% PS ≤1 and 19% non-smokers; 88% had adenocarcinoma. PD-L1 was positive in 85% (n=4 missing). Median PFS was 17.5 months (mo.) (95%CI, 13.2-24.9) and mOS 47 mo. (95%CI, 47-not reached [NR]). No statistically significant differences in terms of mPFS were observed between dGA vs. non-dGA pts: 14.9 mo. (95%CI, 8.1-NR) vs. 18 mo. (95%CI, 13.4-28.3) ($P=1.0$); mOS was immature. Median PFS and OS rate at 18 mo. by each dGA are detailed in the table. Table: 1172MO

	PFS mo. (95%CI)	OS rate at 18 mo. % (95%CI)
Overall dGA	14.9 (8.1-NR)	93.4 (84.7-100)
<i>KRAS</i> m <i>KRAS</i> m G12C	NR (14.9-NR)NR (11.3-NR)	89.7 (76.8-100)87.5 (67.3-100)
<i>EGFR</i> m <i>EGFR</i> mdel19/ex21	9 (5.8-NR)8.1 (5.8-NR)	100 (NR-NR)100 (NR-NR)
<i>BRAF</i> m <i>BRAF</i> mV600E	3.9 (3.9-NR)8.4 (3.9-NR)	100 (NR-NR)100 (NR-NR)
<i>ALK</i> r	7.8 (7.7-NR)	100 (NR-NR)

Within dGA pts, neither OS nor PFS were correlated with PD-L1 expression, whereas PFS was positively associated with smoking status: 19.2 mo. (95%CI, 11.3-NR) vs. 5.8 mo. (95%CI, 3.9-NR) in non-smokers ($P=0.001$).

Conclusions

We observed limited activity of durvalumab consolidation in pts with stage III non-resectable NSCLC with dGA, except for those harbouring *KRAS*m. Larger studies are needed to confirm these findings.

Legal entity responsible for the study

The authors.

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Disclosure

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Pilotto: Financial Interests, Institutional, Funding, Lectures: Roche; Financial Interests, Institutional, Funding, Lectures: Pfizer; Financial Interests, Institutional, Funding, Lectures: Merck Serono; Financial Interests, Institutional, Funding, Lectures: BMS; Financial Interests, Institutional, Invited Speaker: MSD; Financial Interests, Institutional, Invited Speaker: Lilly; Financial Interests, Institutional, Invited Speaker: Amgen; Financial Interests, Institutional, Invited Speaker: Boehringer Ingelheim; Financial Interests, Institutional, Invited Speaker: AstraZeneca; Financial Interests, Institutional, Invited Speaker: Takeda. M. Tagliamento: Financial Interests, Institutional, Other: Roche; Financial Interests, Institutional, Other: Bristol Myers Squibb; Financial Interests, Institutional, Other: AstraZeneca; Financial Interests, Other: Takeda; Financial Interests, Writing Engagements: Novartis; Financial Interests, Writing Engagements: Amgen. E. Nadal: Financial Interests, Funding, Lectures: Roche; Financial Interests, Funding: Pfizer; Financial Interests, Funding, Lectures: Merck Serono; Financial Interests, Funding, Lectures: BMS; Financial Interests, Advisory Board: MSD; Financial Interests, Advisory Board: Lilly; Financial Interests, Advisory Board: Amgen; Financial Interests, Advisory Board: Boehringer Ingelheim; Financial Interests, Advisory Board: AstraZeneca; Financial Interests, Advisory Board: Takeda. D. Signorelli: Financial Interests, Institutional, Advisory Role: AstraZeneca; Financial Interests, Institutional, Advisory Role: Boehringer Ingelheim; Financial Interests, Institutional, Advisory Role, Other: Merck Sharp & Dohme; Financial Interests, Institutional, Other: Roche; Financial Interests, Institutional, Other: Bristol Myers Squibb. 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: BioGene; Financial Interests, Institutional, Sponsor/Funding: Blueprint Medicines; Financial Interests, Institutional, Sponsor/Funding: BMS; Financial Interests, Institutional, Sponsor/Funding: Boehringer Ingelheim; Financial Interests, Institutional, Sponsor/Funding: Celgene; Financial Interests, Institutional, Sponsor/Funding: Cristal Therapeutics; Financial Interests, Institutional, Sponsor/Funding: Daiichi Sankyo; Financial Interests, Institutional, Sponsor/Funding: Eli Lilly; Financial Interests, Institutional, Sponsor/Funding: GSK; Financial Interests, Institutional, Sponsor/Funding: Ignyta; Financial Interests, Institutional, Sponsor/Funding: Ipsen; Financial Interests, Institutional, Sponsor/Funding: Inivata; Financial Interests, Institutional, Sponsor/Funding: Janssen; 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: OSE Immunotherapeutics; Financial Interests, Institutional, Sponsor/Funding: Pfizer; Financial Interests, Institutional, Sponsor/Funding: PharmaMar; Financial Interests, Institutional, Sponsor/Funding: Roche-Genentech; Financial Interests, Institutional, Sponsor/Funding: Sanofi; Financial Interests, Institutional, Sponsor/Funding: Servier; Financial Interests, Institutional, Sponsor/Funding: Spectrum Pharmaceuticals; Financial Interests, Institutional, Sponsor/Funding: Takeda; Financial Interests, Institutional, Sponsor/Funding: Tiziana Pharma; Financial Interests, Institutional, Sponsor/Funding: Tolero Pharmaceuticals. D. Planchard: Financial Interests, Institutional, Advisory Role, Lectures, Clinical Research, Honoraria, other: AstraZeneca; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research: Bristol Myers Squibb; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research: Boehringer Ingelheim; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research: Celgene; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research: Daiichi Sankyo; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research: Eli Lilly; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research, Other: Merck; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research, Other: Novartis; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Other: prIME Oncology; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria: Peer CME; Financial Interests, Institutional, Advisory Role, Lectures, Honoraria, Clinical Research, Other: Roche; Financial Interests, Institutional, Principal Investigator: MedImmune; Financial Interests, Institutional, Principal Investigator: Sanofi-Aventis; Financial Interests, Institutional, Principal Investigator: Taiho Pharma; Financial Interests, Institutional, Principal Investigator: Novocure. 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