2021 ESMO congress

1732MO
Pembrolizumab and nintedanib for patients with advanced mesothelioma

F-X. Danlos[1], C. Baldini[2], A. Varga[2], S. Mouraud[3], B. Job[4], D. Letourneur[5], L. Cassard[6], D. Bredel[5], S. Laghouati[7], M. Texier[8], J. Adam[9], N. Droin[10], A. Parpaleix[11], N. Chaput[12], A. Rabeau[13], G. Zalcman[14], D. Planchard[15], C. Massard[16], J-C. Soria[17], A. Marabelle[18]

[1] INSERM U1015 - Drug Development Department, Gustave Roussy, Paris Saclay University, Villejuif, France, [2] Drug Development Department (DITEP), Gustave Roussy, Villejuif, France, [3] INSERM U1015 - Drug Development Department, Gustave Roussy, Villejuif, France, [4] Bioinformatics Core Facility, INSERM US23, CNRS UMS 3655, Gustave Roussy, Villejuif, France, [5] INSERM UMR1015, Gustave Roussy, Villejuif, France, [6] Laboratory of Immunomonitoring in Oncology, CNRS-UMS 3655 and INSERM-US23, Paris Saclay University, Gustave Roussy, Villejuif, France, [7] Pharmacovigilance Department, Gustave Roussy, Villejuif, France, [8] Biostatistics, Institut Gustave Roussy, Villejuif, France, [9] Pathology Dept., Groupe Hospitalier Paris Saint Joseph, Paris, France, [10] Genomic Core Facility, INSERM US23, CNRS UMS 3655, Gustave Roussy, Villejuif, France, [11] Gustave Roussy, Villejuif, France, [12] Laboratory of Immunomonitoring in Oncology, UMR9019 - CNRS, Genome Integrity and Cancers, Equipe labellisée Ligue Nationale Contre le Cancer, Université Paris-Saclay, Gustave Roussy, Villejuif, France, [13] Unité d'Oncologie Cervico-Thoracique, Centre Hospitalier Universitaire de Toulouse - Hopital Larrey, Toulouse, France, [14] Thoracic Oncology Department, Institution Université de Paris, Hôpital Bichat, APHP, Paris, France, [15] Medical Oncology Department, Gustave Roussy, Villejuif, France, [16] Drug Development Department (DITEP), Gustave Roussy, Villejuif, France, [17] Institut Gustave Roussy, Villejuif, France[18] Drug Development Department, INSERM U1015-LRTI, Paris Saclay University, Gustave Roussy, Villejuif, France

Background

We report the results from the advanced malignant mesothelioma (aMM) expansion cohort of the PEMBIB phase Ib trial (NCT02856425) evaluating the safety, efficacy & biomarkers of an antiangiogenic TKI (nintedanib = [N]) with an anti-PD1 immunotherapy (pembrolizumab = [P]).

Methods

Patients (Pts) with aMM that relapsed after at least one line of platinum-based combination were treated with a combination of oral [N] (150mg BID) & IV [P] (200mg Q3W) with 7 days [N] lead-in preceded [P] initiation. Baseline and on-treatment fresh tumor & blood samples were prospectively phenotyped immune cells by flow cytometry (FC). RNAseq was run on tumor samples. Immune factors were titrated by multiplex ELISA on tumor secretome and plasma.

Results

30 aMM Pts were treated and 29 evaluable for response. Median age was 68 years old (38-85) and 86% of aMM were epithelioid. The most frequent adverse events (AE) (grades 1-3) related to the combination were liver enzymes increase, fatigue, nausea and diarrhea. 4 (13.3%) Pts developed grade 3-5 immune- related AE. Patients died of cancer progression (n=14), myocarditis with thrombo-embolic event (n=1) and COVID-19 (n=1). Median follow-up was 14.8 months (95%CI [9.70-18.2]). Best Overall Response Rates (BORR) were Partial Response (PR; n=7), Stable Disease (SD; n=17) and Progressive Disease (PD; n=5). Disease Control Rate (DCR) (defined as PR + SD) was 68.4% and 46.6% at 3 and 6 months, respectively. Analyses on *fresh* tumor biopsies showed that all patients increased their CD3+ T-cells and circulating levels of soluble PD1 and CXCL9 under treatment. Pts developing PR had significantly higher CD45+ and CD3+ tumor infiltrative cells at baseline compared to Pts with SD & PD as BORR. Pts with DCR at 6 months had significantly higher expression of integrins on circulating effector memory $CD4^+$ & $CD8^+$ T cells by FC, and higher NK, T, and myeloid dendritic cells infiltrates on baseline tumor RNAseq. Pre & on-treatment IL6 and IL8 levels in tumor secretome & plasma were higher among Pts with PD.

Conclusions

With a BORR of 23% and a DCR of 47% at 6 months, [P]+[N] combination provided valuable therapeutic benefits for Pts with aMM. Flow cytometry and secretome on fresh baseline tumor biopsies are simple techniques which could be used to predict treatment efficacy in aMM Pts.

Clinical trial identification

NCT02856425.

Legal entity responsible for the study

Gustave Roussy.

Funding

Funding: Boehringer Ingelheim; Drug supply: Boehringer Ingelheim & MSD; Sponsor: Gustave Roussy.

Disclosure

C. Baldini: Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Institutional, Research Grant: Seattle Genetics; Financial Interests, Institutional, Research Grant: Iteos; Financial Interests, Institutional, Invited Speaker: Tahio; Financial Interests, Institutional, Research Grant: BMS. N. Chaput: Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: BMS; Financial Interests, Institutional, Research Grant: GSK; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Institutional, Research Grant: Sanofi; Financial Interests, Institutional, Research Grant: Cytune Pharma. G. Zalcman: Financial Interests, Personal, Invited Speaker, outside the submitted work: BMS; Financial Interests, Personal, Invited Speaker, outside the submitted work: MSD; Financial Interests, Personal, Invited Speaker, outside the submitted work: AstraZeneca; Financial Interests, Personal, Invited Speaker, outside the submitted work: Boehringer Ingelheim; Non-Financial Interests, Personal, Advisory Board, outside the submitted work: Roche; Non-Financial Interests, Personal, Advisory Board, outside the submitted work: Takeda; Non-Financial Interests, Personal, Advisory Board, outside the submitted work: AstraZeneca; Non-Financial Interests, Personal, Advisory Board, outside the submitted work: AbbVie. C. Massard: Non-Financial Interests, Personal, Advisory Role: Amgen; Non-Financial Interests, Personal, Advisory Role: Astellas Pharma; Non-Financial Interests, Personal, Advisory Role: AstraZeneca; Non-Financial Interests, Personal, Advisory Role: Bayer; Non-Financial Interests, Personal, Advisory Role: BeiGene; Non-Financial Interests, Personal, Advisory Role: BMS; Non-Financial Interests, Personal, Advisory Role: Celgene; Non-Financial Interests, Personal, Advisory Role: Debiopharm Group; Non-Financial Interests, Personal, Advisory Role: Genentech/Roche; Non-Financial Interests, Personal, Advisory Role: Ipsen; Non-Financial Interests, Personal, Advisory Role: Janssen; Non-Financial Interests, Personal, Advisory Role: Lilly; Non-Financial Interests, Personal, Advisory Role: MSD; Non-Financial Interests, Personal, Advisory Role: Novartis; Non-Financial Interests, Personal, Advisory Role: Pfizer; Non-Financial Interests, Personal, Advisory Role: Sanofi; Non-Financial Interests, Personal, Advisory Role: Orion; Non-Financial Interests, Personal, Advisory Role: Taiho Pharmaceuticals; Non-Financial Interests, Personal, Advisory Role: Blueprint Medicinces; Non-Financial Interests, Personal, Advisory Role: Innate Pharma; Non-Financial Interests, Personal, Advisory Role: PharmaMar; Non-Financial Interests, Personal, Advisory Role: Faron Pharmaceuticals. J-C. Soria: Financial Interests, Personal, Stocks/Shares: AstraZeneca; Financial Interests, Personal, Stocks/Shares: Gritstone Oncology; Financial Interests, Personal, Stocks/Shares: Relay Therapeutics; Financial Interests, Personal, Member of the Board of Directors: Hookipa Pharmaceuticals; Financial Interests, Personal, Full or part-time Employment, sept 2017 to dec 2019: AstraZeneca. A. Marabelle: Financial Interests, Personal, Invited Speaker: Roche/Genentech; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: Merck Serono; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Invited Speaker: Amgen; Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Invited Speaker: Servier; Non-Financial Interests, Personal, Principal Investigator: Roche/Genentech; Non-Financial Interests, Personal, Principal Investigator: BMS; Non-Financial Interests, Personal, Principal Investigator: MSD; Non-Financial Interests, Personal, Principal Investigator: Pfizer; Non-Financial Interests, Personal, Principal Investigator: Lytix Pharma; Non-Financial Interests, Personal, Principal Investigator: Eisai; Non-Financial Interests, Personal, Principal Investigator: AstraZeneca; Non-Financial Interests, Personal, Principal Investigator: Tesaro; Non-Financial Interests, Personal, Principal Investigator: Chugai; Non-Financial Interests, Personal, Principal Investigator: Ose Immunotherapeutics; Non-Financial Interests, Personal, Principal Investigator: Sotio; Non-Financial Interests, Personal, Principal Investigator: Molecular Partners; Non-Financial Interests, Personal, Principal Investigator: IMCheck; Non-Financial Interests, Personal, Principal Investigator: Pierre Fabre; Non-Financial Interests, Personal, Principal Investigator: Adlai Nortye; Financial Interests, Personal, Stocks/Shares: Pegascy SAS; Financial Interests, Personal, Stocks/Shares: Centessa Pharmaceuticals; Financial Interests, Personal, Stocks/Shares: HiFiBio; Financial Interests, Personal, Stocks/Shares: Shattuck Labs; Financial Interests, Institutional, Research Grant: Merus; Financial Interests, Institutional, Research Grant: BMS; Financial Interests, Institutional, Research Grant: Boehringer Ingelheim; Financial Interests, Institutional, Research Grant: Transgene; Financial Interests, Institutional, Research Grant: Fondation MSD Avenir; Financial Interests, Institutional, Research Grant: Sanofi. All other authors have declared no conflicts of interest.