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Analysis of the phase 2 part of IFCT-2103 DIAL phase 2-3 randomized trial, comparing continuation pembrolizumab ($\pm$ pemetrexed) up to 2 years versus observation ($\pm$ pemetrexed), in patients with metastatic non-small cell lung cancer (mNSCLC) with disease control (DC) at 6 months

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Background

Optimal duration of 1L immunotherapy (io) in mNSCLC patients. with DC remains debatable. We aimed to study de-escalation by stopping pembrolizumab in patients with 6-months DC after chemo-io induction, as compared to 24 months.

Methods

This randomized open-label trial included treatment-naïve 18-75 yrs. mNSCLC patients (pts), ECOG PS 0-1, w/o actionable tumor molecular alteration, stratified according to PS, histology (SCC. vs. non-SCC), PD-L1 tumor level, sex and quality of response (stable vs. objective response). They received 4 cycles of 1L platinum-based chemo doublet+pembro, either paclitaxel-carboplatin, followed by maintenance pembro, for SCC patients or pemetrexed-platinum, followed by pembro + pemetrexed continuation for non-SCC patients. At 6 months, patients with DC were randomized 1:1 either to pembrolizumab ($\pm$ pemetrexed in non-SCC patients) continuation until 2 years, or to observation ($\pm$ pemetrexed). Primary outcome was 18-mo. overall survival (OS) from inclusion. Secondary outcomes included safety from randomization.

Results

From May 2022 to March 2024, 197 patients (68.0% male, 63.3y median age, 66% stage IVB, 70.6% adenocarcinoma), were accrued. 93 (47.2%) patients were randomized: to the continuation control arm (n=47) or the de-escalation arm (n=46). In Dec. 2025, the phase II analysis involved 84 first eligible patients (42 in each arm). Both arms were well balanced according to clinical and biological characteristics. Median follow-up was 27.9 months 95%CI [25.0 - 31.1]. At 18 months, 83.3%, 95%CI [72.1 - 94.6] were alive in the continuation arm vs. 88.1%, 95%CI [78.3 - 97.9] in the de-escalation arm. In the 93 randomized patients, grade 3-4 rates from randomization were 14.9% and 6.5%, while all-grade irAEs were 85.1% and 47.8%, in the continuation arms and the de-escalation arms, respectively.

Conclusions

In patients with 6-mo DC, similar rates of 18-mo OS were observed in both arms, while leading to lower frequency of irAEs in the de-escalation arm. Accrual in the trial phase 3 part is continuing.

Clinical trial identification

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Legal entity responsible for the study

Intergruppe Francophone de Cancérologie Thoracique.

Funding

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Disclosure

A.C. Toffart: Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, Janssen, MSD, Novocure, Pfizer, Roche, Takeda; Financial Interests, Personal, Invited Speaker: AstraZeneca, BMS, Roche, Takeda. C. Mascoux: Financial Interests, Personal, Invited Speaker: AstraZeneca, Roche, Bristol Myers Squibb, Pfizer, MSD, Amgen, Janssens; Financial Interests, Personal, Advisory Board: MSD, AstraZeneca, Roche, Bristol Myers Squibb, Pfizer, Kephren, Janssens, Takeda, Sanofi, Novartis, Regeneron. J. Cadranet: Financial Interests, Personal and Institutional, Local PI: AstraZeneca, Amgen, BMS, MSD, J&J/Janssen, Roche, Pfizer, Takeda; Financial Interests, Personal and Institutional, Other, Congress/traveling: MSD, Pfizer, Takeda. M. De Wolf: Financial Interests, Personal, Advisory Board: AstraZeneca, Roche, MSD, Amgen; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb International, Sanofi, Pfizer, Johnson and Johnson. D. Debieuvre: Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, MSD, Janssen, Amgen, Roche, Chugai, Pfizer; Financial Interests, Institutional, Funding: Roche, AstraZeneca, Janssen, MSD, Pfizer, BMS, Lilly, Chugai, Takeda, Bayer, Sanofi-Winthrop, Amgen, AbbVie, Regeneron, Novocure, Pierre Fabre. A. Lemoine: Financial Interests, Institutional, Invited Speaker: Pfizer, MSD, AstraZeneca, Daiichi Sankyo, Johnson and Johnson, Amgen; Non-Financial Interests, , Principal Investigator: Novartis, Lilly, AnHeart Therapeutics, MSD, AstraZeneca, Pfizer. E. Pons-Tostivint: Financial Interests, Personal, Advisory Board: AstraZeneca, Takeda, BMS, Sanofi, Roche, Daiichi Sankyo, Amgen, Janssen; Financial Interests, Institutional, Local PI: AstraZeneca, BMS, Daiichi Sankyo, Sanofi, PDC Line, Takeda, Amgen, Janssen. T. Chatellier: Financial Interests, Personal, Other, Travel reimbursement: AstraZeneca, Bristol Myers Squibb, Merck Sante SAS, MSD France SAS. A.B. Cortot: Financial Interests, Personal, Invited Speaker: AstraZeneca, AstraZeneca, MSD, Pfizer, Takeda, Roche, Pierre Fabre; Financial Interests, Personal, Advisory Board: Roche, Pfizer, Janssen, Exelion, Amgen, Pierre Fabre; Financial Interests, Institutional, Research Grant: Merck, Roche, AbbVie, Exelion; Financial Interests, Institutional, Coordinating PI: AstraZeneca; Financial Interests, Institutional, Local PI: Janssen, Roche, Sparta, Amgen, Mirati, AbbVie; Non-Financial Interests, Member of Board of Directors: French Thoracic Intergroup. All other authors have declared no conflicts of interest.

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