

LBA76

Paclitaxel-bevacizumab ± atezolizumab in advanced non-squamous NSCLC progressing after chemo-immunotherapy: IFCT-2201 ADAPTABLE randomized phase II trial

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Background

Options are limited beyond chemo-immunotherapy (CT-IT) in advanced stage, non-squamous non-small cell lung cancer (nSq NSCLC) without oncogenic driver. Addition of anti-angiogenic agents improves taxane efficacy. Whether combining paclitaxel/bevacizumab (P/B) with atezolizumab (A) could have a synergistic effect to overcome resistance to IT in NSCLC remains undetermined.

Methods

Open-label, randomized (2:1), non-comparative, multicenter phase II trial, in PS 0-1 nSq NSCLC pts, progressing after CT-IT (arm A: P/B; arm B: A/P/B; 21-day cycles; no crossover allowed). Stratification by treatment line (2nd vs 3rd), PD-L1 status (<1% vs 1-49 vs ≥ 50%) and time to disease progression (DP) with previous IT (<6 vs ≥6 months). Primary endpoint was progression-free survival (PFS) at 6 months, assessed by independent review committee (IRC). Secondary endpoints were PFS by investigators, objective response rate (ORR), overall survival (OS), safety and quality of life.

Results

From 04/2023 to 08/2024, 168 pts were enrolled in 42 centers (males: 64%, median age: 63.6 yrs, adenocarcinoma: 88%, PD-L1 negative status: 44%, brain metastasis: 27%, only 1 previous line: 90%). Five pts were untreated mostly due to DP or intercurrent event; 10 pts were deemed ineligible. Primary endpoint, 6-month PFS by IRC in eligible pts was 52.0% [95%CI: 38.2-65.9] in arm A (n=50), and 40.8% [31.3-50.3] in arm B (n=103); 6-month PFS by investigators was 52.0% [95%CI: 38.2-65.9] and 42.7% [33.2-52.3], respectively. Median PFS was 7.5 months in arm A [95%CI: 5.8-9.8] and 6.2 months in arm B [5.5-8.2]. ORR was 42.0% in arm A and 41.7% in arm B. Median OS was 17.0 months [95%CI: 10.9-NR] in arm A and 16.6 months [10.8-19.3] in arm B. Grade 3-4 toxicities occurred in 26.4% arm A pts and 28.1% arm B pts; grade 5 rate was 9.4% and 9.1%. No unexpected toxicity was reported. Subgroup analyses according to stratification factors, KRAS or KEAP1/STK11 status, did not modify the findings.

Conclusions

P/B was prospectively confirmed as a good salvage treatment after CT-IT, reinforcing its value in routine, whilst addition of atezolizumab to P/B failed to further improve patient outcome in this setting; both regimens without new safety signal.

Clinical trial identification

EU CT: 2022-502103-30-00 (authorised 16/02/2023); NCT05781308.

Legal entity responsible for the study

Interroupe Francophone de Cancérologie Thoracique (IFCT).

Funding

Interroupe Francophone de Cancérologie Thoracique (IFCT); Roche France.

Disclosure

A. Scherpereel: Financial Interests, Personal, Advisory Board: BMS, Astra-Zeneca, MSD, Leo Pharma; Financial Interests, Personal, Invited Speaker: BMS, Astra-Zeneca, MSD; Financial Interests, Institutional, Coordinating PI: BMS; Non-Financial Interests, Personal, Training, Invitation to international oncology meetings: Astra-Zeneca, MSD, BMS; Non-Financial Interests, Personal, Training, invitation to international oncology meeting: Amgen. L. Greillier: Financial Interests, Personal, Advisory Board: AbbVie, AstraZeneca, BMS, MSD, Novartis, Sanofi, Takeda, Roche, Daiichi Sankyo, Johnson and Johnson; Financial Interests, Personal, Invited Speaker: Lilly, Pfizer, Regeneron; Financial Interests, Institutional, Local PI: AstraZeneca, AbbVie, BMS, MSD, Novartis, Takeda, Pfizer, Roche, PharmaMar, Johnson and Johnson, Boehringer Ingelheim; Financial Interests, Institutional, Coordinating PI: Sanofi, Daiichi Sankyo, Amgen. V. Gounant: Financial Interests, Personal, Speaker's Bureau: Regeneron, BMS, AstraZeneca, Takeda, Amgen, Pfizer; Financial Interests, Personal, Other, Support for attending meetings /travel: Takeda, Pfizer, Regeneron. S. hiret: Financial Interests, Institutional, Advisory Board: BMS, Takeda, AstraZeneca, Sanofi, Roche; Financial Interests, Institutional, Other, support for attending meeting: Novartis; Financial Interests, Institutional, Other, support for WCLC Congress: PharmaMar. L. Bigay-Game: Financial Interests, Personal, Invited Speaker: MSD, AstraZeneca, BMS, Pfizer; Financial Interests, Personal, Advisory Board: Janssen-Cilag, Takeda, Novocure. C. Mascaux: 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. S. Couraud: Financial Interests, Institutional, Research Grant, HCL: Adene, Canon, BD, Transdiag, Volition, Sophia Genetics; Financial Interests, Institutional, Research Grant, HCL, ARISTOT: AstraZeneca, BMS, Roche; Financial Interests, Institutional, Research Grant, ARISTOT: Chugai, I Medica, Janssen, Lilly, MSD, Pfizer, Pierre Fabre, Regeneron, Sanofi, Takeda, Pharmamar, Amgen; Financial Interests, Personal, Expert Testimony: Amgen, AstraZeneca, BMS, Boehringer, Chugai, Fabentech, Health Event, Janssen, MaaT Pharma, MSD, Novartis, Pierre Fabre, Roche, Sanofi, Takeda; Financial Interests, Personal, Other, Support for attending meetings/travel: AstraZeneca, Amgen, Laidet, Pfizer, BMS, Chiesi, Janssen, Roche, Takeda; Non-Financial Interests, Personal, Non remunerated activity, Member of executive committee: Adene, Société de Pneumologie de Langue Française; Non-Financial Interests, Personal, Non remunerated activity, Member of scientific committee: Ensemble nous poumons; Non-Financial Interests, Personal, Non remunerated activity, Member: Lung Cancer policy network; Non-Financial Interests, Personal, Non remunerated activity, President: Association de Recherche et d'Information Scientifique en Oncologie Thoracique (ARISTOT); Financial Interests, Personal, Other, Consulting physician: SNCF. O. Bylicki: Financial Interests, Personal, Advisory Board, Expert Board: BMS, Roche, Takeda; Financial Interests, Personal, Other, Travel congress: MSD; Financial Interests, Personal, Advisory Board, expert board: Astra-Zeneca, Janssen; Financial Interests, Personal, Advisory Board, Board: MSD; Financial Interests, Personal, Other, Travel Congress: Astra-Zeneca. P. Fournel: Financial Interests, Personal, Advisory Board: BMS, MSD; Financial Interests, Personal, Invited Speaker: Astra-Zeneca, Amgen, Sanofi; Financial Interests, Personal, Other, Congress invitation: Takeda. V. Westeel: Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, Pfizer; Financial Interests, Personal, Other, scientific committee and invited speaker: MSD; Financial Interests, Personal, Invited Speaker, and scientific committee: Roche, Amgen; Financial Interests, Personal, Invited Speaker, and board: Sanofi; Financial Interests, Institutional, Other, local PI: Bristol Myers Squib; Financial Interests, Institutional, Coordinating PI: MSD, Merck; Financial Interests, Institutional, Local PI: Roche, Daiichi, Amgen, Seagen, Ose Immunotherapeutics; Other, Other, support for meeting attendance: AstraZeneca, Bristol Myers Squib, Janssen; Other, Other, Support for meeting attendance: MSD, Amgen. E. Giroux-Leprieur: Financial Interests, Personal, Advisory Role: AstraZeneca, Boehringer-Ingelheim, Bristol-Myers-Squib, Janssen, Lilly, MSD, Pfizer, Roche, Sanofi, Takeda; Financial Interests, Personal, Other, Support for attending meetings/travel: Roche, Pfizer; Financial Interests, Personal, Other, Support for attending meeting: Takeda. All other authors have declared no conflicts of interest.