BERLIN 2025 ESMO congress

LBA110

A blinded, exploratory phase II trial of nivolumab and the GDF-15 neutralizing antibody visugromab or placebo as neoadjuvant treatment of patients with muscle-invasive bladder cancer (MIBC): Primary results of the GDFather-NEO trial

A. Necchi[1], C. Mercinelli[1], B.A. Maiorano[1], V. Tateo[1], R. Iacovelli[2], C. Ciccarese[2], C. Ligato[2], P. Giannatempo[3], A. Rametta[3], P. Gontero[4], F. Soria[4], C. Schuberth-Wagner[5], J. Wischhusen[6], A. Amin[7], F. Hermann[7], A. Kamova[8], K. Klar[8], A. Auckenthaler[7], E. Leo[7], F.S. Lichtenegger[7]

[1] Medical Oncology Dept., IRCCS Ospedale San Raffaele, Milan, Italy, [2] Medical Oncology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [3] Department of Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, [4] Division of Urology, Department of Surgical Sciences, University of Torino, Turin, Italy, [5] Research & Discovery, CatalYm GmbH, Planegg-Martinsried, Germany, [6] Obstetrics and Gynecology, University of Würzburg, Wuerzburg, Germany, [7] Clinical Development, CatalYm GmbH, Planegg-Martinsried, Germany[8] Translational Research, CatalYm GmbH, Planegg-Martinsried, Germany

Background

Neoadjuvant chemotherapy in MIBC suffers from limited activity and significant toxicity. Anti-PD-(L)1 monotherapy achieved comparable pathologic complete response (pCR) rates and improved tolerability. Growth and Differentiation Factor 15 (GDF-15) was recently identified as a key mediator of resistance to PD-(L)1 blockade in metastatic solid tumors [*Nature 2025; 637, 1218ff*].

Methods

The multicenter GDFather-NEO trial (NCT06059547) investigated visugromab (V; aGDF-15; 20 mg/kg) in combination with nivolumab (N; aPD-1; 480 mg) vs. N + placebo (P), administered Q4W for 3 cycles in cisplatin-ineligible/refusing participants (pts) with newly diagnosed clinical stage T2-T4aN0M0 MIBC. Pts were centrally stratified for PD-L1 CPS and cT-stage. Radical cystectomy or re-transurethral resection of the bladder tumor (TURBT) was performed 4-8 wks after last dose. Key endpoints were pCR (ypT0), major pathologic response (MPR, ypT<=1) and radiologic objective response rate (ORR; RECIST v1.1).

Results

Of 31 pts enrolled between September 2023 and March 2025, 28 were efficacy-evaluable (15 for N/V, 13 for N/P). 6 and 3 underwent re-TURBT post-treatment in N/V and N/P arms, respectively. Regarding efficacy, pCR (33.3 vs. 7.7%) and MPR (66.7% vs. 23.1%) rates were substantially higher for N/V vs. N/P. ORR as per RECIST v1.1 was 60.0% (7xCR/2xPR) vs. 15.4% (0xCR/2xPR) for N/V vs. N/P. N/V was superior across all T stages and dominantly in CPS≥10%. Tolerability of N+V was very good, detailed safety data will be shown. Baseline serum GDF-15 levels were comparable between N/V (n=13; mean 1.491 ng/mL; range 0.385 – 4.212 ng/mL) and N/P (n=10; mean 1.400 ng/mL; range 0.644 – 3.326ng/mL).

Conclusions

In anti-PD(L)-1-naïve MIBC, GDF-15 blockade by visugromab tripled the effect size of nivolumab in neoadjuvant therapy, with excellent tolerability. N/V combination warrants further investigation in larger neoadjuvant trials with a tumor response-guided bladder preservation approach.

Clinical trial identification

NCT06059547.

Legal entity responsible for the study

Catalym.

Funding

Catalym.

Disclosure

A. Necchi: Financial Interests, Institutional, Research Grant: Merck, AstraZeneca, Ipsen, BMS, Gilead; Financial Interests, Personal, Steering Committee Member: Janssen, Astellas, AstraZeneca, Merck, Gilead, BMS, Bicycle Therapeutics, Daiichi Sankyo; Financial Interests,

Coordinating PI: Incyte, Genenta Sciences; Financial Interests, Personal, Coordinating PI: Catalym; Financial Interests, Personal, Funding: Samsung Bioepis; Non-Financial Interests, Leadership Role: Global society of Rare Genitourinary Tumors (GSRGT). R. Iacovelli: Financial Interests, Personal, Advisory Board: BMS, MSD, Janssen, Astellas, Ipsen, Pfizer, Bayer, Sanofi, Eisai, Merck, GENENTA; Financial Interests, Personal, Invited Speaker: RECORDATI; Financial Interests, Institutional, Research Grant: BMS; Financial Interests, Institutional, Local PI: MSD, Seagen, Aveo; Non-Financial Interests, Member: AIOM; Non-Financial Interests, Advisory Board, Italian Society of Uro-Oncology: SIUrO. C. Ciccarese: Financial Interests, Personal, Advisory Board: msd, BMS, AstraZeneca; Financial Interests, Personal, Invited Speaker: Astellas, Ipsen, Johnson and Johnson, Novartis; Financial Interests, Personal, Other, travel grant: Pfizer. P. Giannatempo: Financial Interests, Personal, Advisory Role: Astellas, AstraZeneca, Janssen, Merck, Pfizer; Financial Interests, Institutional, Research Funding: AstraZeneca, Ipsen, Merck. P. Gontero: Financial Interests, Personal, Advisory Role: Photocure, Pfizer, Medac, Ferring, AstraZeneca, Merck, MSD; Financial Interests, Personal, Research Funding: Ab medica, Ferring. F. Soria: Financial Interests, Personal, Advisory Role: Medac Pharma S.r.l., Photocure, Pfizer; Financial Interests, Personal, Invited Speaker: Medac Pharma S.r.l. C. Schuberth-Wagner: Financial Interests, Personal, Full or part-time Employment: CatalYm; Financial Interests, Personal, Stocks or ownership: CatalYm, RNhale, Merck Inc. J. Wischhusen: Financial Interests, Personal, Stocks/Shares: CatalYm; Financial Interests, Personal, Advisory Role: CatalYm; Financial Interests, Personal, Royalties: Catalym. A. Amin,F. Hermann, A. Kamova, K. Klar, A. Auckenthaler, F.S. Lichtenegger: Financial Interests, Personal, Full or part-time Employment: CatalYm. E. Leo: Financial Interests, Personal, Full or part-time Employment, CMO: CatalYm GmbH; Financial Interests, Institutional, Stocks/Shares: Catalym GmbH. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology