BERLIN 2025 ESMO congress

LBA95

Neoadjuvant immunotherapy in locally advanced clear cell renal cell carcinoma at risk for recurrence or distant metastases: The randomized phase II NESCIO trial

F. Burgers[1], A. de Ruijter[2], N.M. Graafland[3], M. van Montfoort[4], M. Lopez-Yurda[5], P. Hagen[5], P. Zondervan[6], S. Rynja[7], M. Yska[8], A. Ruiter[9], A. Minnee-van Leeuwen[10], R. de Vries[11], B. Lagerveld[9], D.J. Vis[2], S. Wilgenhof[1], H.V. van Thienen[1], C.U. Blank[1], K. van der Mijn[1], A. Bex[12], J.B.A.G. Haanen[1]

[1] Department of Medical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands, [2] Department of Molecular Carcinogenesis, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands, [3] Department of Urology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands, [4] Department of Pathology, Netherlands Cancer Institute, Amsterdam, Netherlands, [5] Department of Biometrics, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands, [6] Department of Urology, Amsterdam UMC, locatie VUmc, Amsterdam, Netherlands, [7] Department of Urology, Spaarne Hospital Haarlem, Haarlem, Netherlands, [8] Department of Urology, Maasstad Hospital, Rotterdam, Netherlands, [9] Department of Urology, OLVG, Amsterdam, Netherlands, [10] Department of Urology, Hospital St Jansdal, Harderwijk, Netherlands, [11] Urology, Reinier de Graaf Hospital, Delft, Netherlands[12] Department of Urology, Royal Free London NHS Foundation Trust, London, United Kingdom

Background

The standard of care for patients (pts) with intermediate- to high-risk localized clear cell renal cell carcinoma (ccRCC) is surgical resection. Recently, adjuvant pembrolizumab was shown to reduce risk of relapse and improve overall survival. In melanoma, neoadjuvant ICI has superior efficacy compared to adjuvant ICI. Therefore, neoadjuvant ICIs warrant further investigation in ccRCC.

Methods

NESCIO is a randomized, non-comparative, open-label, three-arm, two-stage phase 2 trial in pts with resectable intermediate- to high-risk ccRCC. Pts were randomized to receive two cycles of nivolumab 360 mg (arm A), ipilimumab 1 mg/kg + nivolumab 3 mg/kg (arm B), or nivolumab 360 mg + relatlimab 360 mg (arm C), all q3wks, followed by a CT-scan and nephrectomy. The primary endpoint was pathologic response rate. Secondary endpoints included safety, objective response rate (ORR) per RECIST 1.1, surgical morbidity (Clavien-Dindo), EFS and RFS.

Results

Between Apr 2022 and Feb 2025, 43 pts were included, of which 42 (14 per arm) evaluable for the primary endpoint. Baseline characteristics were balanced between arms. In total, 97.7% of tumors were ≥T3, 25.6% N+, and 51.2% ≥ grade 2. Pathologic response rates were 7.1% in arm A (1 partial pathologic response (pPR)), 14.3% in arm B (2 near-complete pathologic responses), and 14.3% in arm C (1 pPR and 1 complete pathologic response). ORR were 0% in arm A, 7.1% in arm B (1 partial response), and 0% in arm C. Most pts (95.2%) had stable disease. One pt (arm A) had progressive disease prior to surgery. Grade ≥3 immune-related (IR) adverse events were seen in 6.7% in arm A, 42.8% in arm B and 14.2% in arm C. Surgery was delayed >2 wks due to IR toxicity in one pt (arm A). Grade III-IV surgical complications occurred in 0% in arm A, 7.1% in arm B and 14.2% in arm C. RNA sequencing was performed on 40 baseline and 41 post-treatment samples for translational analyses.

Conclusions

Six wks of neoadjuvant ICI resulted in acceptable toxicity and remarkable pathologic responses in a limited number of pts with intermediate- to high-risk ccRCC. Future analyses of survival outcomes and translational data will be pivotal to evaluate efficacy and predictive biomarkers of neoadjuvant ICI in ccRCC.

Clinical trial identification

NCT05148546, Registered December 8, 2021.

Legal entity responsible for the study

Netherlands Cancer Institute.

Funding

Bristol Myers Squibb.

Disclosure

S. Wilgenhof: Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb, MSD; Financial Interests, Institutional, Other, travel expenses: Ipsen. C.U. Blank: Financial Interests, Personal, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre, Third Rock Ventures, Senya; Financial Interests, Institutional, Research Funding: BMS, Novartis, Nanostring, 4SC; Financial Interests, Personal, Stocks or ownership: Flindr Therapeutics; Financial Interests, Personal, Stocks or ownership, WO 2021/177822 A1 (pending), US 2023/0114276 A1 (pending), EP 4114450 A1 (pending), WO 2023/022596 A1 (pending), US (submitted not published yet), EP 4387683 A1 (pending): Patent. K. van der Mijn: Financial Interests, Institutional, Invited Speaker: Novartis; Financial Interests, Institutional, Advisory Board: MSD, AstraZeneca; Financial Interests, Personal, Other, travel compensation: Ipsen; Financial Interests, Personal, Full or part-time Employment: The Netherlands Cancer Institute; Financial Interests, Institutional, Research Grant: Bayer; Financial Interests, Institutional, Local PI: AstraZeneca, MSD. A. Bex: Financial Interests, Institutional, Advisory Board, Online advisory board: Ipsen; Financial Interests, Personal, Advisory Board: Telix; Financial Interests, Institutional, Research Grant, Restricted educational grant for an investigator initiated trial of neoadjuvant therapy in high risk renal cancer: Pfizer; Non-Financial Interests, Principal Investigator, Steering committee member and PI in an adjuvant trial: Roche/Genentech; Non-Financial Interests, Principal Investigator, Steering committee member and local investigator in an adjuvant trial: BMS; Non-Financial Interests, Advisory Role, Medical Steering committee member to advise the patient advocacy group on medical topics and strategy: International Kidney Cancer Coalition, KIdney Cancer Association; Non-Financial Interests, Leadership Role, Chair of the EAU Renal Cancer guidelines: European Association of Urology. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squipp, Achilles Therapeutics, Immunocore, Gadeta, Ipsen, Merck Sharpe & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Instil Bio, Iovance Biotherapeutics, AstraZeneca; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Sastra Cell Therapy; Financial Interests, Personal, Advisory Board: Third Rock Venture, Scenic, CureVac, Imcyse; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharpe & Dohme, Amgen, Novartis, Asher Bio, Sastra Cell Therapy; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Other, Editor-in-Chief IOTECH: ESMO; Other, Other, Editorial Board ESMO Open: ESMO; Other, Other, Editorial Board: Kidney Cancer. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology