

7230

Post-surgical liquid biopsy-guided treatment of stage III and high-risk stage II colon cancer patients: Final results of the PEGASUS trial

S. Marsoni¹, M. Prisciandaro², N. Tarazona Llaveró³, C. Montagut Viladot⁴, A. Sartore Bianchi⁵, M.G. Zampino⁶, F.J. Ros Montana⁷, C. Santos Vivas⁸, M. Mandalà⁹, S. Tamberi¹⁰, M.S. Sciallero¹¹, S. Muñoz¹², P. Luraghi¹, L. Lazzari¹, E. Rulli¹³, V. Torri¹⁴, E. Elez Fernandez⁷, A. Bardelli¹⁵, S. Siena⁵, S. Lonardi¹⁶

¹ Precision Oncology Unit, IFOM ETS - The AIRC Institute of Molecular Oncology, Milan, Italy, ² Department of Medical Oncology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy, ³ Department of Medical Oncology, INCLIVA Biomedical Research Institute, University of Valencia, Instituto de Salud Carlos III, CIBERONC, Valencia, Spain, ⁴ Department Medical Oncology, Hospital del Mar - Parc de Salut Mar, Barcelona, Spain, ⁵ Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, and Grande Ospedale Metropolitano Niguarda, Milan, Italy, ⁶ Division of Gastrointestinal Medical Oncology and Neuroendocrine Tumors, IEO - European Institute of Oncology IRCCS, Milan, Italy, ⁷ Department of Medical Oncology, Vall d'Hebron University Hospital, and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, ⁸ Medical Oncology, ICO - Institut Català d'Oncologia l'Hospitalet (Hospital Duran i Reynals), L'Hospitalet de Llobregat, Spain, ⁹ Department of Medical Oncology, Santa Maria Misericordia Hospital, University of Perugia, Perugia, Italy, ¹⁰ Department of MEDICAL Sciences (DIMEC) University of Bologna, Oncology Unit, Santa Maria delle Croci Hospital - AUSL Romagna, Ravenna, Italy, ¹¹ Medical Oncology Unit 1, IRCCS Ospedale Policlinico San Martino, Genoa, Italy, ¹² VHIO academic CRO, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, ¹³ Oncology Department, Istituto di Ricerche Farmacologiche Mario Negri - IRCCS, Milan, Italy, ¹⁴ Clinical Oncology, Istituto di Ricerche Farmacologiche Mario Negri - IRCCS, Milan, Italy, ¹⁵ Department of Oncology, IFOM ETS - The AIRC Institute of Molecular Oncology, and Molecular Biotechnology Center, University of Torino, Turin, Italy ¹⁶ Medical Oncology Unit 1, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy

Background

Prognostic impact of circulating tumor DNA (ctDNA) positivity on colon cancer disease relapse after radical resection and adjuvant chemotherapy has been previously demonstrated. Here we present the final analysis on the primary endpoint of the PEGASUS trial, designed to investigate the feasibility of using liquid biopsy (LB) to guide the post-surgical and post-adjuvant clinical management of Stage III and T4N0 Stage II colon cancer patients (pts).

Methods

LB was performed using Guardant Reveal assay (v L1.2). In the post-surgical phase, LB+ pts received 3 months of CAPOX and LB- pts 6 months of CAPE. To mitigate the risk of false negatives, after one cycle of CAPE a second LB was performed and if positive the treatment was escalated to CAPOX. At the end of the adjuvant treatment, LB was repeated: CAPOX-treated patients were switched to FOLFIRI if LB+ or de-escalated to CAPE if LB-; CAPE-treated patients received CAPOX if LB+ or standard follow-up if LB-. Primary objective was feasibility of the LB-based strategy, defined as the rate of pts free of disease at 2 years among those with two consecutive post-surgical LB- results. With one-sided $\alpha=0.05$ and 80% power, <14 relapses among 134 LB- pts were required to exclude $H_0=85\%$ in favor of $H_1=92\%$. A matched comparison with TOSCA Trial pts was planned as a secondary endpoint.

Results

From July 2020 to July 2022, 135 pts (100 LB-, 35 LB+) were included from 11 clinical cancer centers in Italy and Spain. At a median follow-up of 33.5 months, 12 relapses occurred among LB- pts, yielding a 2-year NED rate of 88% (90% CI, 81–93). The predefined threshold was not met, but the point estimate exceeded 85% and the confidence interval extended beyond 92%, indicating promise but statistical uncertainty. Within the 35 LB+ pts, 13 (37%) relapses were observed. 2-years time-to-relapse rate was 87.6% in LB- and 61.5% in LB+ (HR 3.22, 95% CI 1.20–7.96, $p=0.0013$).

Conclusions

PEGASUS showed the operational feasibility of ctDNA-guided treatment in stage III and high-risk stage II resected colon cancer. This approach has the potential to reduce unnecessary toxicity by tailoring adjuvant therapy to molecular risk. A historical comparative analysis with pts from the TOSCA trial is ongoing as per-protocol key secondary endpoint.

Clinical trial identification

IFOM-CPT005/2019/PO004; EudraCT 2019-002074-32; EudraCT 2024-517704-10-00; NCT04259944.

Legal entity responsible for the study

IFOM ETS - the AIRC Institute of Molecular Oncology.

Funding

Guardant Health.

Disclosure

S. Marsoni: Other, Institutional, Research Grant: MSD, AstraZeneca, Illumina. N. Tarazona Llaveró: Financial Interests, Personal, Advisory Board: Merck, Guardant Health, Grifols; Financial Interests, Personal, Invited Speaker: MERCK, Pfizer, Servier, Amgen; Financial Interests, Institutional, Funding: Natera Inc, Guardant Health; Non-Financial Interests, Member: SEOM Committee. C. Montagut Viladot: Financial Interests, Personal, Advisory Board: Merck Serono, Roche, Takeda; Financial Interests, Personal, Invited Speaker: Merck Serono, Pierre Fabre, Guardant Health, Amgen, Pfizer, MSD; Financial Interests, Institutional, Invited Speaker: MSD; Financial Interests, Institutional, Royalties: Biocartis; Financial Interests, Institutional, Coordinating PI: Merck-Serono; Non-Financial Interests, Member: TTD (Grupo Tratamiento Tumores Digestivos). A. Sartore Bianchi: Financial Interests, Personal, Invited Speaker: Amgen, Bayer, Pierre Fabre; Financial Interests, Personal, Advisory Board: Servier, Takeda. M.G. Zampino: Financial Interests, Personal, Advisory Board, Advisory Board for discussing the role of dostarlimab in rectal cancer: GSK. F.J. Ros Montana: Financial Interests, Institutional, Invited Speaker: Sanofi; Financial Interests, Personal, Invited Speaker: Pfizer, BMS, Takeda, Johnson and Johnson, Merck, Amgen; Other, Travel and accommodation expenses and Speaker: Amgen, Merck; Other, Travel and accommodation expenses: Pierre Fabre, Sanofi. C. Santos Vivas: Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Invited Speaker: Amgen, Takeda Pharmaceuticals; Other, Travel grant: Merck, MSD, Amgen, Takeda Pharmaceuticals. M. Mandalà: Financial Interests, Personal, Advisory Board: MSD, Novartis, Sanofi, BMS, Pierre Fabre; Financial Interests, Personal, Invited Speaker: Sun Pharma. S. Tamberi: Other, Personal, Speaker, Consultant, Advisor: AstraZeneca, Roche, Incute, Servier, Takeda. M.S. Sciallero: Financial Interests, Personal, Invited Speaker: MSD, Gentili; Financial Interests, Personal, Other, Consultancy on Lynch Syndrome: GSK; Other, Registration/Travel/accommodation expenses for congress: Novartis. S. Muñoz: Financial Interests, Institutional, Full or part-time Employment: Vall Hebron Institut d'Oncologia (VHIO); Financial Interests, Institutional, Other, Head of Academic CRO managing clinical trials: AstraZeneca Spain; Financial Interests, Institutional, Other, Head of academic CRO managing clinical trials: Roche, Bristol Myers Squibb, The Lymphoma Academic Research Organization, Leukos; Financial Interests, Institutional, Other, Head of CRO managing clinical trials: Pfizer, Pierre Fabre, Merck; Non-Financial Interests, Institutional, Product Samples, Head of academic CRO managing clinical trials: Merck, Leukos, Pierre Fabre, Pfizer, Roche, AstraZeneca, Bristol Myers Squibb, The Lymphoma Academic Research Organization. P. Luraghi: Financial Interests, Personal, Full or part-time Employment: AstraZeneca. E. Rulli: Financial Interests, Institutional, Research Grant, Roche supported an investigator initiated trial ,coordinated by our group: Roche; Financial Interests, Institutional, Research Grant, AstraZeneca supported investigator initiated trials, coordinated by our group: AstraZeneca. V. Torri: Financial Interests, Institutional, Funding, Roche supported an investigator initiated trial, coordinated by our department: Roche; Financial Interests, Institutional, Research Grant, AstraZeneca supported with unrestricted grant a study coordinated by our department: AstraZeneca. E. Elez Fernandez: Financial Interests, Personal, Advisory Board: Agenus Inc., Amgen, Bayer, Boehringer Ingelheim, Cure Teq AG, Hoffman La - Roche, Janssen, MSD, Merck Serono, Pierre Fabre, RIN Institute Inc., Repare Therapeutics Inc., Sanofi, Servier, Takeda, Johnson & Johnson, Rottapharm Biotech, Nordic Group BV; Financial Interests, Personal, Invited Speaker: BMS, Lilly, Medscape, Novartis, Organon, Pfizer; Financial Interests, Personal, Other, Steering Committee: GSK; Financial Interests, Personal, Other, Educational training: Seagen International GmbH; Financial Interests, Institutional, Funding: AbbVie Deutschland GmbH & Co KG, Amgen Inc., Array Biopharma Inc, AstraZeneca Pharmaceuticals LP, Bayer Pharma AG, BeiGene, Bioncotech Therapeutics, S.L., Biontech Rna Pharmaceuticals GMBH, BioNTECH Small Molecules GMBH, Boehringer Ingelheim, Boehringer Ingelheim de España S.A., Bristol Myers Squibb International Corporation, Celgene International SARL, Daiichi Sankyo, Inc, Debiopharm International SA, Genentech Inc, Gercor, HalioDX SAS, Hoffmann-La Roche Ltd, Hutchinson Medipharma Limited, Hutchison MediPharma International, Iovance Biotherapeutics, Inc., Janssen Research & Development, Janssen-Cilag SA, MedImmune, Menarini, Menarini Ricerche SPA, Merck Health KGAA, Merck Sharp & Dohme de España SA, Merus NV, Mirati, Nouscom SRL., Novartis Farmacéutica SA, Pfizer, PharmaMar SA, Pledpharma AB, Redx Pharma PLC, Sanofi Aventis Recherche & Développement, Scandion Oncology, Seattle Genetics Inc., Servier, Sotio A.S., Taiho Pharma USA Inc, Wntresearch AB, Exelixis Inc., GSK, SA, Agenus, Nu Cana plc, Enterome BioScience SA; Non-Financial Interests, Leadership Role, Member of the Scientific Program Committee and Developmental Therapeutics-Immunotherapy Track Leader, 2023-2024 term: American Society for Clinical Oncology (ASCO); Non-Financial Interests, Other, Speaker of the ESMO Academy: European Society for Medical Oncology (ESMO); Non-Financial Interests, Other, Member of the Scientific Committee 2024: European Society for Medical Oncology (ESMO); Non-Financial Interests, Other, Coordinator of the SEOM +MIR Section of Residents and Young Assistants: Sociedad Española de Oncología Médica (SEOM); Non-Financial Interests, Other, Member of the Scientific Committee SEOM Annual Meeting, 2024-2025 term: Sociedad Española de Oncología Médica (SEOM); Non-Financial Interests, Member: American Society of Clinical Oncology (ASCO), American Association for Cancer Research (AACR), Sociedad Española de Oncología Médica (SEOM), Asociación Española de Investigación sobre el Cáncer (ASEICA), European Organization for Research and Treatment of Cancer (EORTC), Spanish Cooperative Gastrointestinal Tumors Group (TTD); Other, Travel, accommodations, expenses.: Agenus Inc., Amgen, BMS, Bayer, Boehringer Ingelheim, Cure Teq AG, GSK, Hoffman La-Roche, Janssen, Lilly, MSD, Medscape, Merck Serono, Novartis, Organon, Pfizer, Pierre Fabre, RIN Institute Inc., Repare Therapeutics Inc., Sanofi, Seagen, Servier, Takeda. A. Bardelli:

Financial Interests, Personal, Other, Receipt of honoraria or consultation fees: Guardant Health; Financial Interests, Personal, Advisory Board, Scientific Advisory Board: Neophore; Financial Interests, Personal, Stocks/Shares, Stock shareholder: Neophore, Kither; Financial Interests, Institutional, Research Grant, Receipt of grants/research supports: Neophore, AstraZeneca, Boehringer Ingelheim. S. Siena: Financial Interests, Personal, Advisory Board, Advisory Board Member: Agenus, AstraZeneca, BMS, Checkmab, Daiichi Sankyo, GSK, Novartis, Seagen, T-One-Therapeutics, Merck, MSD. S. Lonardi: Financial Interests, Personal, Advisory Board: Amgen, Merck Serono, Lilly, Servier, AstraZeneca, MSD, Incyte, Daiichi Sankyo, Bristol Myers Squibb, Astellas, GSK, Takeda, Bayer, Rottapharm, BeiGene, Nimbus Therapeutics, Helion; Financial Interests, Personal, Invited Speaker: Pierre Fabre, GSK, Roche, Servier, Amgen, Bristol Myers Squibb, Incyte, Lilly, Merck Serono, MSD, AstraZeneca; Financial Interests, Institutional, Coordinating PI: Amgen, Merck Serono, Bayer, Roche, Lilly, AstraZeneca, Bristol Myers Squibb; Non-Financial Interests, Member of Board of Directors, Italian No-Profit Oncology Research Foundation supporting academic Clinical trials: GONO Foundation. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*