

Table: 129eP Study population

TILs		<20%	≥20%
		N (%)	N (%)
Tumor subtype	Lum	14 (78)	4 (22)
	HER2+	6 (75)	2 (25)
	TNBC	3 (75)	1 (25)
Grade	1	1 (100)	0 (0.0)
	2	14 (82)	3 (18)
	3	8 (73)	3 (27)
EFS		HR 1.74 (95% CI 0.41-7.45), p= 0.46	
OS		HR 1.66 (95% CI 0.26-10.44), p=0.59	
Subgroup analysis for EFS	Lum	HR 0.43 (95% CI 0.04-4.68), p=0.49	
	HER2+	Ref	
	TNBC	HR 2.45 (95% CI 0.15-39.7), p= 0.53	

Conclusions: In our study, most pts experienced a reduction in TILs following NACT. Although exploratory, baseline TILs were not associated with survival outcomes. These findings warrant further investigation to clarify the role of pregnancy-related immunotolerance in shaping the tumor microenvironment.

Legal entity responsible for the study: VHIO.

Funding: Has not received any funding.

Disclosure: M. Perachino: Other, Other, Travel grant: Lilly, Novartis, Daiichi-Sankyo. G. Villacampa: Financial Interests, Personal, Invited Speaker, Invited speaker in a course: MSD; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Invited Speaker, Invited speaker in an internal training: Pierre Fabre, GSK; Financial Interests, Personal, Invited Speaker, Internal discussion about the interpretation of some published results: Pfizer; Financial Interests, Personal, Other, Collaborations with specific projects: Reveal Genomics. M. Gaudio: Other, Other, Congress attendance support: Lilly, Ipsen. E. Zamora Adelantado: Financial Interests, Personal, Invited Speaker, Review session for medical oncologists: Eisai, Lilly, Lilly, Pfizer; Financial Interests, Personal, Invited Speaker, Management of iCDK toxicities to oncologist nurses.: Novartis; Financial Interests, Personal, Advisory Board, Review the evidence of Pembrolizumab in triple negative breast cancer: MSD; Financial Interests, Personal, Invited Speaker, 2 review sessions for medical oncologist from Mexico: Lilly; Financial Interests, Personal, Invited Speaker, Preceptorship MSD - Triple Negative Breast Cancer: MSD; Financial Interests, Personal, Invited Speaker, Investigator Meeting Camizestrant Ophthalmic Safety Study: AstraZeneca; Financial Interests, Personal, Invited Speaker, Review session for Breast Unit: Lilly; Financial Interests, Personal, Invited Speaker, Camizestrant Ophthalmic Safety Study: AstraZeneca; Other, Other, Registration to ESMO Congress 2022 (virtual): Novartis; Other, Other, Registration to: Eisai; Other, Other, Virtual registration to ASCO Congress 2023: Novartis; Other, Other, Registration to SEOM Congress 2023: Lilly; Other, Other, Registration to ESMO Breast Cancer Congress 2023: MSD; Other, Other, Registration to ESMO Congress (virtual): Roche; Other, Other, Travel, accommodation and registration to SABCS 2024: Pfizer; Other, Other, Registration to ESMO Congress 2024: MSD; Other, Other, Travel, accommodation and registration to ESMO Breast 2024: Gilead; Other, Other, Registration to ESMO Breast Congress 2025 (virtual): Lilly; Other, Other, Registration to ESMO Congress 2025 (virtual): Novartis; Other, Other, Registration to SABCS 2025 (virtual): Lilly. S. Escrivá-de-Romaní: Financial Interests, Personal, Advisory Board: Roche, Daiichi Sankyo/AstraZeneca, Seagen, Pierre-Fabre, Jazz Pharmaceuticals, Reveal Genomics; Financial Interests, Personal, Expert Testimony: COR2ED; Financial Interests, Personal, Invited Speaker: Roche, Daiichi Sankyo/AstraZeneca, Pfizer, Seagen, Novartis; Financial Interests, Personal, Other, Travel grants: Pfizer, Seagen; Financial Interests, Personal, Other, Travel Grants: Daiichi Sankyo; Financial Interests, Institutional, Invited Speaker: Roche, Synthron, Byondis, Lilly, MedSIR, Zymeworks, Daiichi Sankyo/AstraZeneca, SOLTI, Jazz Pharmaceuticals. M. Bellet Ezquerro: Financial Interests, Personal, Advisory Board: Pfizer, Novartis, Lilly, Stemline-Menarini; Other, Other, Speaker's Bureau and Travel Expenses: Pfizer; Other, Other, Speaker's Bureau: Novartis, Lilly. M. Oliveira: Financial Interests, Personal, Advisory Board: AstraZeneca, Daiichi Sankyo, Gilead, Hoffmann-La Roche, Lilly, MSD, Pfizer, ProteinQure, Novartis; Financial Interests, Personal, Invited Speaker: AstraZeneca, Gilead, Lilly, MSD, AstraZeneca, AstraZeneca; Financial Interests, Personal, Other, Honoraria: Curio Science, i-One; Financial Interests, Institutional, Invited Speaker: AstraZeneca, Gilead, Pfizer, Roche, Immute; Non-Financial Interests, Member: AACR, ASCO, SEOM; Non-Financial Interests, Leadership Role, President elected 2023-2027: SOLTI Cancer Research Group; Other, Other, Travel Grant: AstraZeneca, Gilead, Roche, Pfizer. C. Saura Manich: Financial Interests, Personal, Advisory Board: AstraZeneca, Daiichi Sankyo, Eisai, Exact Sciences, Exeter Pharma, F. Hoffmann - La Roche Ltd, Gilead, Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Philips, Pierre Fabre, PintePharma, Puma, Roche Farma, Sanofi-Aventis, SeaGen, Zymeworks, Pharmalex Spain SLU, REVEAL GENOMICS, S.L.; Financial Interests, Personal, Expert Testimony: Boehringer Ingelheim, Bristol Meyers Squibb, Genentech, Innoup, Millenium; Financial Interests, Personal, Other, SC: Byondis B.V., Glaxo, MacroGenics, Menarini, Merus, Synthron Biopharmaceuticals; Financial Interests, Personal, Invited Speaker, Faculty on an EBAC Accredited Medical Education activity: PeerVoice. PSL Group; Financial Interests, Personal, Other, Chair: Aventik Medical S.L.U.; Financial Interests, Institutional, Research Grant: AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Bristol-Myers Squibb (BMS), Cytomx Therapeutics, Daiichi Sankyo, Eli Lilly and Company, F. Hoffmann-La RocheLtd, Genentech, GSK, Immunomedics, Innoup Farma, MacroGenics, Menarini Recherche, Merus, Novartis, Pfizer, Puma, Roche, Sanofi-Aventis, Seattle Genetics; Financial Interests, Institutional, Invited Speaker: Byondis B.V.; Financial Interests, Institutional, Funding, institutional financial interest in form of financial support for clinical trials or contracted research: Amgen, BeiGene, Debiopharm International SA, Janssen-Cilag SA, Merck Health KGAA, Merck Sharp & Dohme, Mirati, Pharma Mar, Servier, Taiho Pharma USA Inc, Spanish Association Against Cancer Scientific Foundation and Cancer Research UK.; Financial Interests, Personal, Research Grant: Cooperative breast cancer group SOLTI; Financial Interests, Personal, Invited Speaker: BN CONGRESS ORGANIZATION S.L.; Non-Financial Interests, Member of Board of Directors: Cooperative breast cancer group SOLTI; Non-Financial Interests, Member: Spanish Society of Medical Oncology (SEOM), American Society for Clinical Oncology (ASCO), Geicam (Spanish Breast Cancer Research Group), European Society for Medical Oncology (ESMO), Sinology Society of the Official College of Physicians of Barcelona (COMB), The European Association for Cancer Research (EACR.), Advisory Board on Cancer Infertility and Pregnancy (ABCIP); Non-Financial Interests, Member, Junta Directiva y Comité Científico: SOLTI group (Academic research group in breast cancer); Other, Other, Member of the Consensus Panelist Group: International multidisciplinary consensus on the integration of radiotherapy with new systemic treatments for breast

cancer: European Society for Radiotherapy and Oncology (ESTRO)-endorsed recommendations.: Consensus Panelist Group; Other, Other, Associate Editor and Peer reviewer Breast Care Journal: Karger Publishers. All other authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107083>

130eP Programmed death-ligand 1 (PD-L1) immunohistochemical expression in triple-negative breast cancer: A clinicopathological study from a tertiary care center in South India

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Background: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype lacking ER, PR and HER2 expression, with limited targeted treatment options. TNBC shows higher immunogenicity with prominent tumor-infiltrating lymphocytes (TILs) and immune checkpoint activation. PD-L1 expression is a predictive biomarker for immune checkpoint inhibitor therapy; however, data from Indian populations are limited. This study evaluated PD-L1 expression in TNBC and its association with clinicopathological features and outcomes.

Methods: This retrospective observational study included 123 TNBC cases diagnosed between 2019–2025. Histological classification and Nottingham grading were performed. TILs, lymphovascular emboli (LVE), nodal status and Ki-67 were assessed. PD-L1 immunohistochemistry was performed using SP263 clone on Ventana BenchMark ULTRA. Tumor cell positivity was defined as ≥5% staining and immune cell positivity as ≥1%. Associations were analyzed using Chi-square test and survival by Kaplan–Meier analysis.

Results: Median age was 51 years; 60.2% were postmenopausal. Most tumors were IBC-NST (92.6%) and grade 3 (60.2%). TILs were present in 66.7%, LVE in 42.2% and nodal metastasis in 43.1%. PD-L1 tumor cell positivity was seen in 26.8% and immune cell positivity in 37.4%. Co-expression occurred in 25.2%. PD-L1 expression showed significant association with LVE (p=0.000) and TILs (p<0.0001), but not with age, stage, size, grade, nodal status or Ki-67. Recurrence occurred in 8.9% and mortality in 22.8%; PD-L1 was not independently prognostic.

Conclusions: PD-L1 expression in TNBC is strongly associated with immune-active tumor microenvironment features, particularly TILs and lymphovascular invasion, rather than traditional prognostic parameters. A substantial subset of Indian TNBC patients demonstrates PD-L1 positivity, supporting the relevance of immune biomarker testing for therapeutic stratification in real-world settings.

Legal entity responsible for the study: The Authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107084>

132eP Paclitaxel-Loaded Silica Nanoparticle Microneedle Arrays Enable Sustained Transdermal Drug Delivery for Localised Breast Cancer Therapy

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Background: Paclitaxel is a cornerstone of breast cancer treatment but is limited by systemic toxicity, particularly peripheral neuropathy. Localised breast cancer involvement, including cutaneous metastases and chest-wall recurrence, represents a setting where targeted drug delivery may improve local tumour control while minimising systemic exposure. Biodegradable microneedle systems offer a minimally invasive platform for transdermal drug administration and may enable localised chemotherapy delivery.

Methods: Paclitaxel-doped silica nanoparticles were synthesised at varying drug-to-carrier ratios and characterised for particle size, surface charge, and polydispersity using dynamic light scattering. Optimised formulations were incorporated into biodegradable carboxymethylcellulose-sugar microneedle arrays. Microneedle morphology and structural integrity were assessed using microscopy. Ex vivo skin penetration was evaluated to confirm delivery to the epidermal-dermal interface, and nanoparticle release behaviour was examined.

Results: Paclitaxel-loaded silica nanoparticles demonstrated nanoscale dimensions, stable negative zeta potentials, and low polydispersity at optimised drug-to-carrier ratios, indicating colloidal stability and uniformity. These nanoparticles were successfully incorporated into dissolvable microneedle arrays without aggregation. The microneedles effectively penetrated the stratum corneum and enabled controlled and sustained nanoparticle release over several hours while maintaining mechanical

integrity and formulation stability within the microneedle matrix, supporting localised transdermal delivery of paclitaxel.

Conclusions: This translational preclinical study demonstrates the feasibility of paclitaxel-loaded nanoparticle microneedle arrays as a localised transdermal drug delivery platform. This approach may represent a targeted therapeutic strategy for localised breast cancer involvement, with potential to reduce systemic toxicity associated with conventional paclitaxel administration. Further preclinical evaluation is warranted to support future clinical translation.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107086>

133eP A multi-modal AI facilitates prognostication of patients with TPBC

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Background: Triple-positive breast cancer (TPBC; ER+/PR+/HER2+) accounts for approximately 10% of breast cancers and is often grouped with HER2-positive disease. However, TPBC represents a highly heterogeneous subtype with diverse clinical and pathological traits, which require complex decisions regarding systemic therapy, notably in stratifying patients for chemotherapy or intensified anti-HER2 treatment. There are currently no guideline-endorsed prognostic or predictive tools specifically developed for patients with TPBC. To address this gap, we evaluated Ataraxis Breast (ATX), a multimodal AI test that integrates clinical information with morphological information from H&E-stained whole slide images, to determine its ability to prognosticate recurrence risk in TPBC.

Methods: ATX scores were generated from H&E-stained slides obtained from FFPE tissue samples from 28 patients with TPBC from Lodz, Poland; no patients in this cohort were used to train ATX. The primary endpoint in this study was recurrence-free interval (RFI). The performance of ATX was assessed using C-index, and its association with outcome was estimated using Cox proportional hazards models, with HRs reported per 0.1 increase in ATX score.

Results: The cohort included 28 patients with confirmed treatment-naïve invasive ductal carcinoma: 12 with stage T1 and 16 with stage T2 disease. Approximately half (n = 15, 54%) of the patients were node negative and tumors were grade 1 (n=3), grade 2 (n = 17), and grade 3 (n=8). Median tumor size was 22.5 mm (IQR = 17.75-30 mm). ATX demonstrated strong discrimination for RFI (C-index = 0.89, 95% CI = 0.67-1.00) and was significantly associated with higher hazard of an RFI-contributing event in a univariate Cox model (HR = 2.78, 95% CI = 1.24-6.24, p-value = 0.01). In a multivariate Cox model adjusting for T stage, nodal status, and grade, ATX remained independently prognostic (HR = 3.84, 95% CI = 1.25-11.79, p-value = 0.02) while T stage, nodal status, and grade were not significant (p > 0.05).

Conclusions: In an independent TPBC cohort, ATX identified patients at increased risk of recurrence. These findings suggest that multimodal AI-based risk stratification may address an unmet prognostic need in TPBC, a population currently lacking a guideline-supported tool.

Legal entity responsible for the study: Medical University of Lodz.

Funding: The project was supported by the National Science Centre (NCN), Poland (Preludium grant no. 2018/29/N/NZ4/02384 and OPUS grant no. 2020/39/B/NZ4/02696), as well as by the National Centre for Research and Development (NCBR), Poland (LIDER programme, contract no. LIDER13/0188/2022).

Disclosure: All authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107087>

134eP The NFYA regulon is associated with basal-like breast cancer phenotypes and influences cell cycle, DNA repair, and replication processes

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Background: The basal-like breast cancer subtype poses a significant clinical challenge; nevertheless, the transcription reprogramming (TR) associated with its phenotypes remains only partially understood. Here, we investigate how the *NFYA*

transcription factor contributes to TR in these tumors and impacts tumor biology and clinical behavior.

Methods: To this end, we employed bioinformatic approaches to identify genes whose expression is influenced by *NFYA* (*NFYA* regulon), predict the processes and pathways in which this regulon is involved, and identify associations between regulon activity and clinical traits. Next, *NFYA* expression was synthetically inhibited using siRNA transfection to evaluate its impact on basal-like cell lines (MDA-MB-231 and MDA-MB-468).

Results: Overexpression of *NFYA* in basal-like tumors vs. non-tumor samples ($P < 0.0001$) was associated with poor overall patient survival ($P = 0.037$). The *NFYA* regulon, comprising 414 genes, was linked to higher tumor mutational burden, mutation score, and Buffa's hypoxia score. Enrichment and GSVA analyses demonstrated its involvement primarily in cell cycle regulation, DNA replication, and DNA repair pathways, among other processes. Consistently, *in vitro* and cytometry analyses demonstrated that *NFYA* silencing reduced cell viability, proliferation, and colony formation, inducing G1-phase cell cycle arrest ($P < 0.05$). Late apoptosis and necrosis were also induced upon *NFYA* silencing ($P < 0.05$). Regarding DNA repair, the comet assay showed that *NFYA* silencing increased DNA damage accumulation ($P < 0.05$) and sensitized cells to X-ray irradiation and doxorubicin treatment ($P < 0.05$). Quantitative PCR corroborates these findings by showing decreased expression of proliferation markers (*MKI67*, *PCNA*) and DNA repair markers (*ATM*, *CHK1*), alongside increased pro-apoptotic *BAX* and decreased anti-apoptotic *BCL-2*.

Conclusions: We demonstrate that *NFYA* modulates TR in basal-like breast tumors and influences biological processes and their aggressive phenotypes. Our findings suggest that targeting *NFYA* could impair tumor progression and sensitize cells to DNA damage-inducing therapies.

Editorial acknowledgement: We used Grammarly as a tool to correct our non-native English.

Legal entity responsible for the study: Federal University of Paraná, Brazil.

Funding: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Ministério da Ciência, Tecnologia e Inovação. Brazil.

Disclosure: All authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107088>

135eP Assessing the added value of tumour-draining vein sampling for liquid biopsy-based genomic profiling in Breast Cancer

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Background: Liquid biopsy offers a minimally invasive approach for detecting tumour-derived genomic alterations in breast cancer, yet the optimal blood sampling site for maximizing diagnostic sensitivity remains unclear. This retrospective study compared the performance of standard peripheral blood collection with selective venous sampling (SVS) from tumour-draining veins to evaluate whether proximity to the tumour enhances mutation detection.

Methods: Plasma-derived cfDNA from 10 breast cancer patients (non-metastatic to metastatic) was analysed. Each patient underwent both peripheral venous sampling and SVS. Comprehensive genomic profiling was performed using the Guardant360 CDx assay, an NGS-based, analytically validated IVD. Variants with MAF > 0.2% were included in the analysis.

Results: Genomic alterations were detected in 6 of 10 patients (60%). Concordance in alteration count between sampling sites was observed in 4 patients (40%). Among discordant cases, SVS identified a greater number of alterations in 2 patients (20%), while peripheral sampling never outperformed SVS (0%). Four patients (40%) had no detectable variants in either sample type.

Conclusions: This preliminary analysis indicates that selective venous sampling may enhance detection of breast cancer-related genomic alterations compared with peripheral sampling in selected cases. A prospective study with adequate sample size is now planned to validate these findings and clarify the clinical utility of tumour-proximal liquid biopsy strategies. *Authors would like to thank Prof. Bruno Damascelli and Dr. Vladimira Tichà of Fondazione Falciani Onlus.

Legal entity responsible for the study: Marina Elena Cazzaniga.

Funding: Has not received any funding.

Disclosure: M.E. Cazzaniga: Financial Interests, Personal, Invited Speaker: PIERRE FABRE; Financial Interests, Personal, Advisory Board: NOVARTIS, MENARINI STEMLINE, GILEAD; Financial Interests, Institutional, Research Grant: ELI LILLY, EISAI. All other authors have declared no conflicts of interest.

<https://doi.org/10.1016/j.esmoop.2026.107089>