Pseudo-Anonymized Non-Interventional Retrospective Clinical Validation of AI-Ambient Patient-Clinical Intelligence (A.P.C.I.) Using the GRADE Methodology

Ivaylo Petrov, PharmD
Dimitar Kalev, Assoc. Prof., MD, PhD
Hristo Ivanov
Constantinos Zamboglou, Prof., MD, MHBA
Abhishek Pathak, Prof., MD, FRCP, DrNB
Assia Konsoulova, Assoc. Prof., MD, PhD

SHEMHA HEALTH

01 / Background

- A fundamentally new approach to **evidence-based clinical decision-making is required for optimizing** and personalizing diagnostic and therapeutic interventions in cancer care. This includes enhancing the effectiveness of multidisciplinary tumor teams (MDTs), **comprehensive cancer efficiency**, clinical practice guidelines, and health policies.

- The World Health Organization (WHO) has endorsed the **GRADE** (Grading of Recommendations Assessment, Development, and Evaluation) approach as the most rigorous and transparent methodology for assessing the quality of evidence and formulating healthcare recommendations.[1] Meanwhile, **generative artificial intelligence (Gen-AI) customization** would provide an efficient and scalable tool for systematically retrieving systematic reviews and analyzing large volumes of statistical parameters to evaluate evidence quality.[2,3]

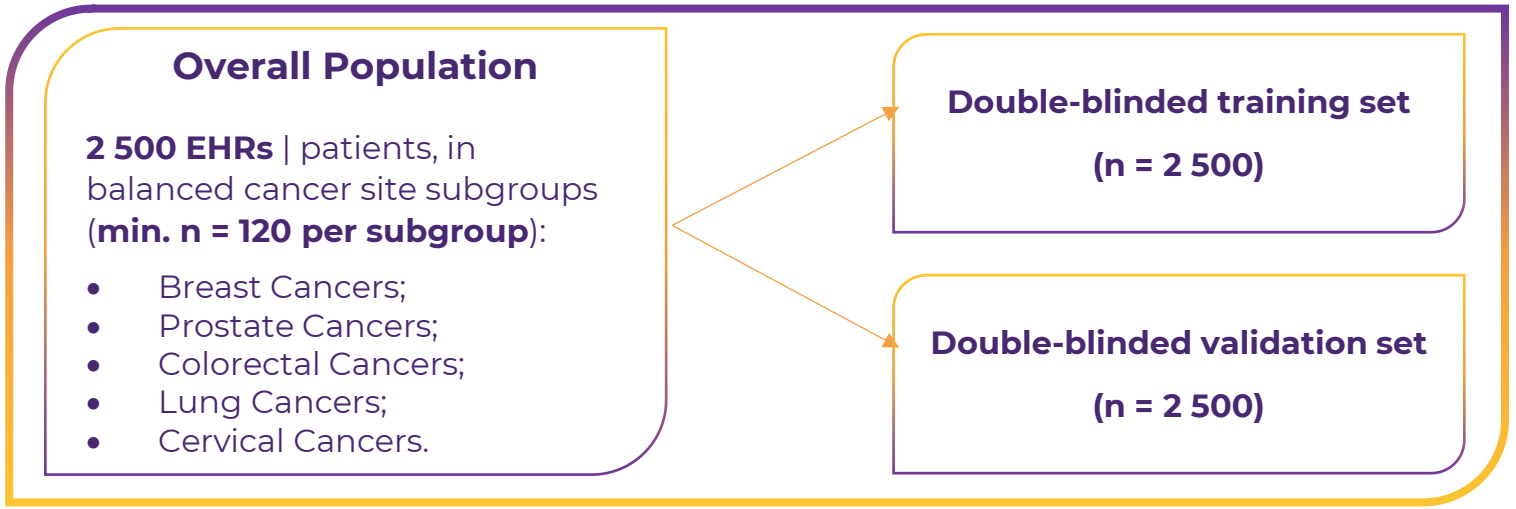
- The **AI-Ambient Patient-Clinical Intelligence (A.P.C.I.)** system, serves as clinical decision-making component of the tele-oncology platform PrOPA. It is designed to support practicing oncologists, MDTs and oncology institutions by leveraging structured **PICO-based clinical questions** and systematically curated, structured, and parameterized **evidence datasets** derived from systematic review publications in digital libraries.

1. *GRADE guidelines; Gordon Guyatt at. all; Journal of Clinical Epidemiology 64 (2011) 383e394*
2. *Huo, B. MD et. al. Large Language Models for Chatbot Health Advice Studies - A Systematic Review, JAMA Network Open. 2025;8(2):e2457879. doi:10.1001/jamanetworkopen.2024.57879*
3. *Wilhelm, C. et. al. Benefits and harms associated with the use of AI-related algorithmic decision-making systems by healthcare professionals: a systematic review. The Lancet Regional Health – Europe 2025;48: 101145. December 2024*

© Shemha Health, 2025

02 / Study Design

NON-INTERVENTIONAL RETROSPECTIVE CLINICAL TRIAL



Algorithm development:

(1) Development of an LLM algorithm for PICO structured clinical questions and GRADE-based recommendations for diagnostic and therapeutic intervention;
(2) Internal testing of the algorithm;
(3) Training using a training set;
(4) Validation using a validation set.

Primary Endpoints

- **Intervention Choice Accuracy**: Training v/s Validation Set;
- **Extent of Agreement (Chance Agreement)**: A.P.C.I. recommendation v/s MDT decision.

Secondary Endpoints

- **Subgroup cost-effectiveness analyses (CEAs)**: Training v/s Validation Set QALY
- **Subgroup overall survival (OS)**: Training v/s Validation Set
- **Subgroup progression free survival (PFS)**: Training v/s Validation Set

Huo, B. MD et. al. Large Language Models for Chatbot Health Advice Studies - A Systematic Review, JAMA Network Open. 2025;8(2):e2457879. doi:10.1001/jamanetworkopen.2024.57879

© Shemha Health, 2025

03 / AI Algorithm and Statistics

Manual Definition

Define patient/population + clinical problem/intervention + target outcome

PICO Structuring

A.P.C.I. Algorithm Structured PICO Question: Patient | Intervention | Comparison | Outcome

Literature Search

Algorithm searches digital libraries for systematic reviews/meta-analysis

Evidence Extraction

Extracts systematic reviews/meta-analyses into GRADE tables

Recommendations

A.P.C.I. formulated recommendations (references summery incl.) for the multidisciplinary tumor boards

Statistical analyses

- Measures of observer variability (Kappa statistic);
- Cox Proportional Hazard (PH) model: Hazard ratio (HR) with 95% confidence interval (95% CI);
- Cost-effectiveness analyses (Quality-Adjusted Life Years).

Metadata analyses:

- Analyzes over **12 million** scientific papers;
- Reviews **2 million** Systematic Reviews;
- Processes over **700 thousand** meta-analyses

The system leverages the entire **PubMed and Cochrane libraries** for evidence-based clinical decision-making.

© Shemha Health, 2025

04 / Patient Characteristics and Inclusion Criteria

The study population will comprise patients diagnosed with malignancies across various sites.

Inclusion criteria:

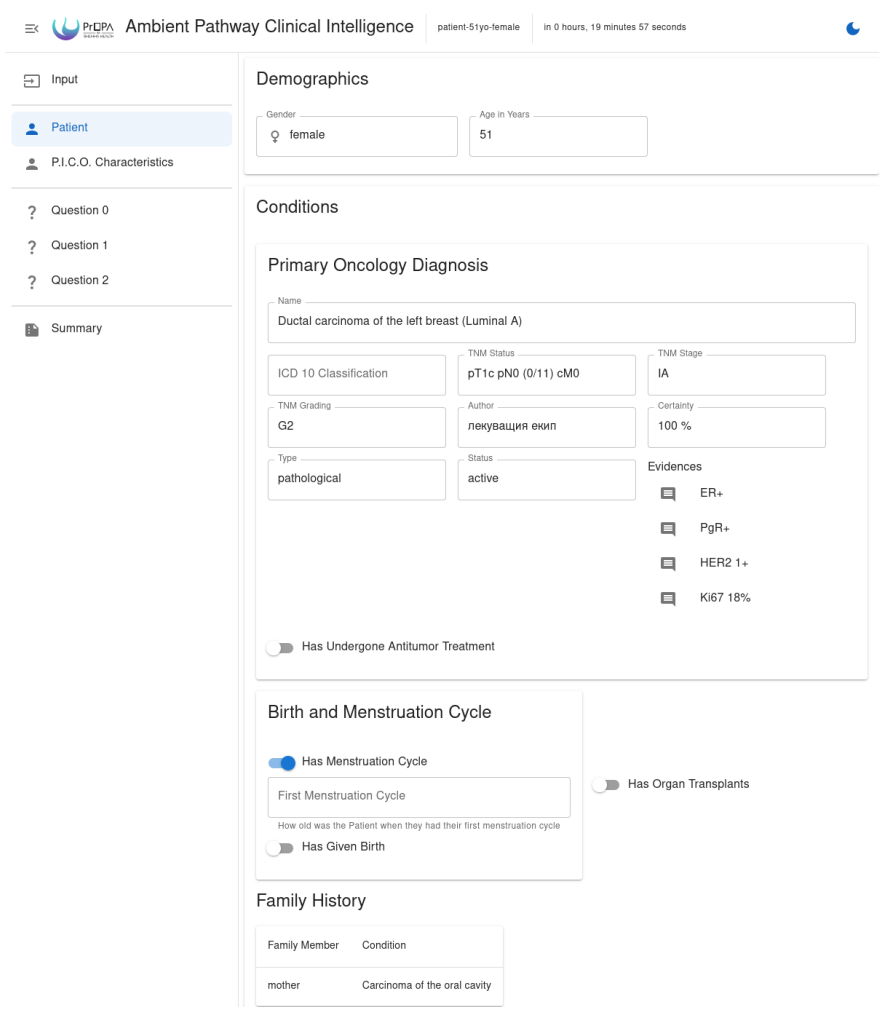
- Patients with available structured and/or unstructured data-sets (**electronic health records (EHRs)**) suitable for analysis. Both baseline and follow-up data are considered valuable for retrospective learning and validation.
- **Follow-up data** (including patient history, diagnostic findings, treatment outcomes, clinical notes, and multidisciplinary tumor board recommendations) are preferred, as they allow for direct comparison between A.P.C.I. artificial system-generated recommendations and human clinical decision-making.
- **Diagnosis confirmed** through **biopsy, pathology, and/or imaging reports**.
- Patients who have **ongoing and/or completed a full course of treatment** with documented clinical outcomes.

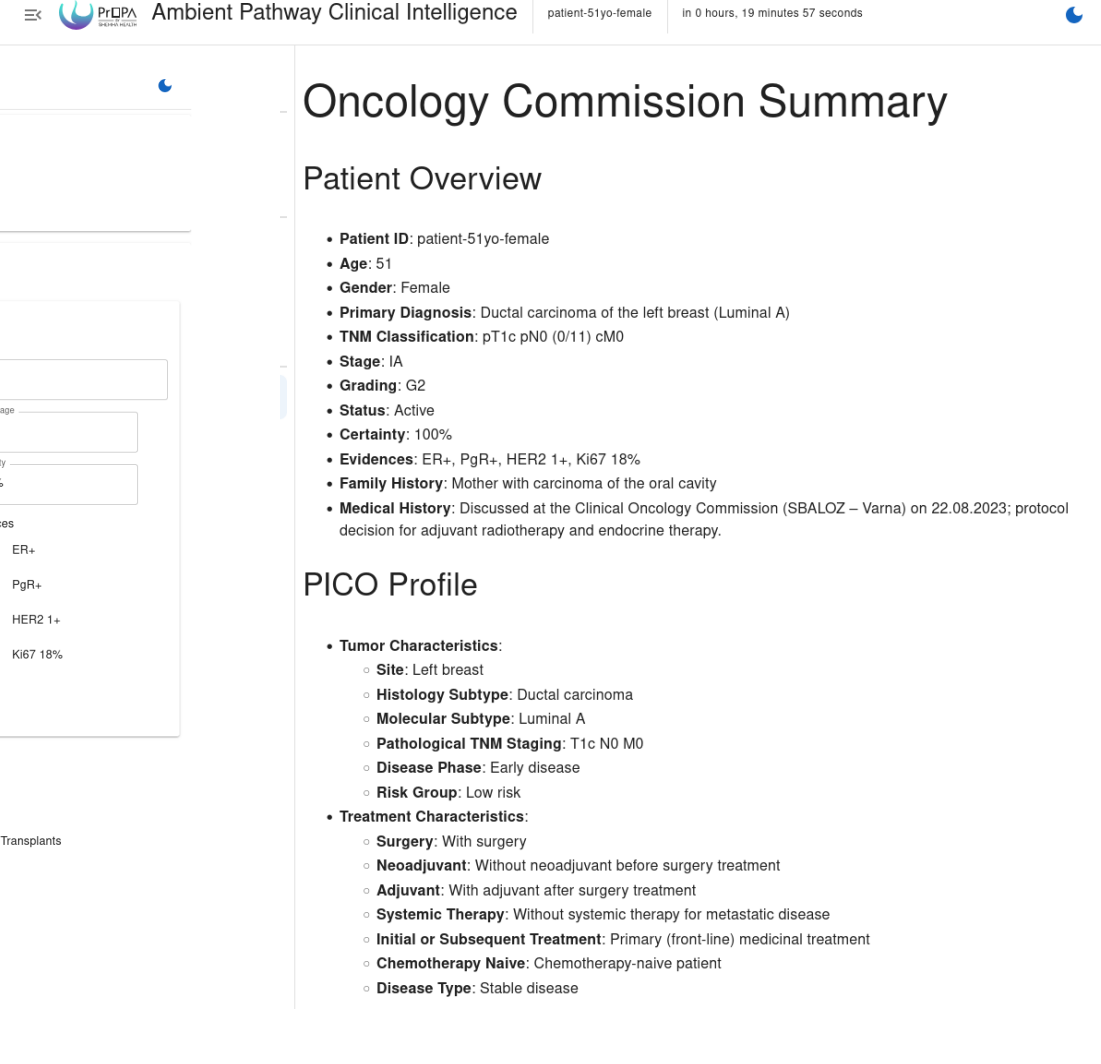
Sites

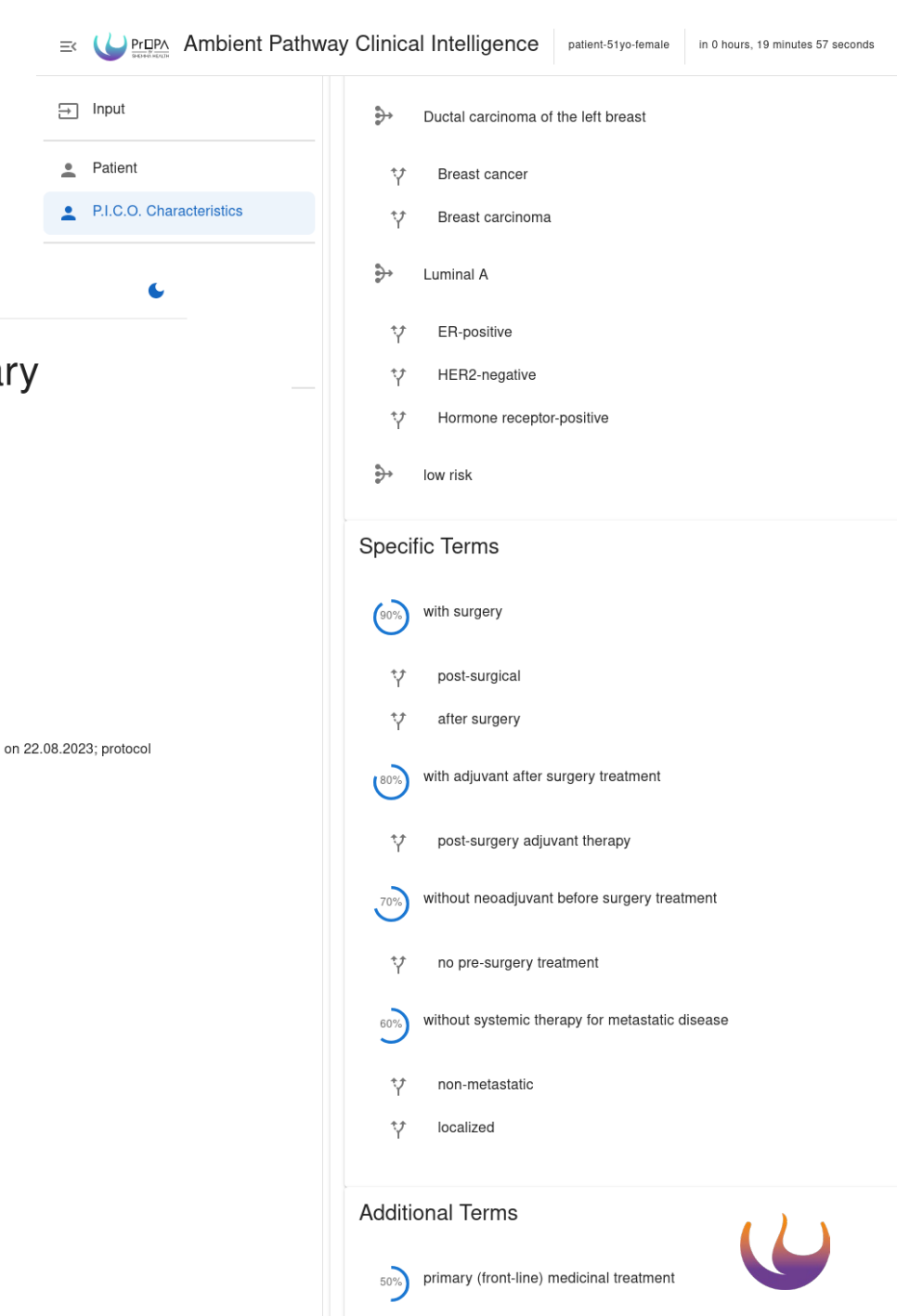
- PrOPA™ existing pseudo-anonymized database
- Bulgarian Cancer Database
- German Cancer Center, Limassol, Cyprus
- Sao Joao Hospital, Porto, Portugal
- Command Hospital Kolkata, Kolkata, India

© Shemha Health, 2025

05 / A.P.C.I. Learning & Results | Case 1







06 / A.P.C.I. Learning & Results | Case 2

Ambient Pathway Clinical Intelligence | patient-51yo-female | in 0 hours, 19 minutes 57 seconds

- Input
- Patient
- P.I.C.O. Characteristics
- P.I.C.O. 1
- P.I.C.O. 2
- P.I.C.O. 3
- Summary

For the patient with ductal carcinoma of the left breast (Luminal A), it is recommended to consider the Oncotype DX 21-gene Recurrence Score (RS) for prognostic evaluation, as it provides valuable insights into locoregional recurrence rates. Additionally, assessing BAG-1 mRNA expression could offer prognostic information regarding breast cancer-specific survival. Tumour-infiltrating lymphocytes (TILs) levels may also be considered, although the evidence quality is lower. These tests can help tailor the treatment plan and predict outcomes more accurately.

Interventions Considered

Reasoning and Evidence

The Oncotype DX 21-gene Recurrence Score (RS) is a valuable prognostic tool for predicting locoregional recurrence rates in estrogen receptor-positive breast cancer.

Value of the 21-gene expression assay in predicting locoregional recurrence rates in estrogen receptor-positive breast cancer: a systematic review and network meta-analysis. (2022-06-01)

Outcome	Certainty of Evidence	Effect Group Size	Control Group Size	Relative Effect (95% CI)	Absolute Effect (95% CI)	No. of Participants
Locoregional recurrence (LRR) rates for each RS category using traditional and TAILORx cut-offs.	◯◯ ◯◯ Very Low	4269	3944	1.76 (1.32 - 2.37)	3.45 (2.63 - 4.53)	8213

Tumour-infiltrating lymphocytes (TILs) levels are associated with local recurrence in non-invasive breast cancer.

Tumour-infiltrating lymphocytes in non-invasive breast cancer: A systematic review and meta-analysis. (2021-10-01)

Outcome	Certainty of Evidence	Effect Group Size	Control Group Size	Relative Effect (95% CI)	Absolute Effect (95% CI)	No. of Participants
Association with local recurrence (invasive or non-invasive)	◯◯ ◯◯ Very Low	3437	2941	2.05 (1.03 - 4.08)		6378

Questions and Answers

Diagnostic Interventions

- **Question**: What are the required diagnostic interventions in their practical sequence?
- **Answer**: No interventions considered relevant for this patient.

Predictive Biomarkers

- **Question**: What are the required testing/diagnostic interventions to identify predictive biomarkers?
- **Answer**:
  - **Oncotype DX 21-gene Recurrence Score (RS)**: Valuable for predicting locoregional recurrence rates in estrogen receptor-positive breast cancer.
    - **Evidence**: Value of the 21-gene expression assay in predicting locoregional recurrence rates in estrogen receptor-positive breast cancer: a systematic review and network meta-analysis.
    - **Quality**: Moderate
  - **Tumour-infiltrating lymphocytes (TILs) levels**: Associated with local recurrence in non-invasive breast cancer.
    - **Evidence**: Tumour-infiltrating lymphocytes in non-invasive breast cancer: A systematic review and meta-analysis.
    - **Quality**: Low
  - **BAG-1 mRNA expression**: Associated with improved breast cancer-specific survival in early breast cancer.
    - **Evidence**: BAG-1 as a biomarker in early breast cancer prognosis: a systematic review with meta-analyses.
    - **Quality**: Moderate

Therapeutic Interventions

- **Question**: What are the required therapeutic interventions in their practical sequence?
- **Answer**:
  - **Adjuvant Endocrine Therapy**: Crucial for improving event-free and overall survival in women with non-metastatic breast cancer.
    - **Evidence**: Importance of endocrine treatment adherence and persistence in breast cancer survivorship: a systematic review.
    - **Quality**: Moderate
  - **Radiotherapy**: Following breast-conserving surgery significantly reduces breast cancer mortality.
    - **Evidence**: Adjuvant and neoadjuvant breast cancer treatments: A systematic review of their effects on mortality.
    - **Quality**: High

This summary provides a comprehensive overview of the patient's condition, recommended diagnostic and therapeutic interventions, and the supporting evidence for these recommendations. The evidence quality and relevance to decision-making have been assessed using the GRADE methodology.

07 / A.P.C.I. Learning & Results | Case 3

Ambient Pathway Clinical Intelligence | in 1 hours, 29 minutes 4 seconds

- Input
- Patient
  - Profile
  - Primary Cancer Diagnosis
  - Original Diagnosis
  - Medical History
- P.I.C.O. Characteristics
- P.I.C.O. 1
- P.I.C.O. 2
- P.I.C.O. 3
- Summary

? For this cancer/tumor site/localization, what are the required therapeutic interventions in their practical sequence?

Based on the provided evidence, the recommended therapeutic sequence for the patient includes adjuvant endocrine therapy with tamoxifen or aromatase inhibitors, followed by radiotherapy to reduce recurrence risk. Additionally, switching to anastrozole after 2-3 years of tamoxifen treatment is advised for improved survival outcomes. These interventions are supported by high-quality evidence and should be implemented in the pat treatment plan.

Interventions Considered

Reasoning and Evidence

Adjuvant endocrine therapy, such as tamoxifen or aromatase inhibitors, is recommended for women with hormone receptor-positive, HER2-negative early breast cancer to improve disease-free survival and reduce recurrence rates.

Radiotherapy following breast-conserving surgery is essential for reducing local recurrence risk in early-sta breast cancer patients.

Switching from tamoxifen to anastrozole after 2-3 years of treatment improves disease-free survival and ev free survival in postmenopausal women with hormone-sensitive early-stage breast cancer.

Medication: Anastrozole

95% Effectiveness of switching from adjuvant tamoxifen to anastrozole in postmenopausal women with hormone-sensitive early-stage breast cancer: a meta-analysis. (2006-12-01)

GRADE Table Summary of Findings

Systematic review/MetaAnalysis:
Effectiveness of switching from adjuvant tamoxifen to anastrozole in postmenopausal women with hormone-sensitive early-stage breast cancer: a meta-analysis.

Patients/Population:
Postmenopausal women with hormone-sensitive early-stage breast cancer
Intervention:
Switching to anastrozole after 2-3 years of tamoxifen
Comparator:
Continuing tamoxifen for a total of 5 years

Outcome	Illustrative Risk		Relative Effect (95% CI)	Number of Participants (Studies)	Overall Quality of Evidence	Comments
	Assumed Risk	Corresponding Risk				
Disease-free survival	NR	NR	HR 0.59 95% CI 0.48 - 0.74	4006 patients (3 RCT)	⨁⨁⨁⨁	
Event-free survival	NR	NR	HR 0.55 95% CI 0.42 - 0.71	4006 patients (3 RCT)	⨁⨁⨁⨁	
Distant recurrence-free survival	NR	NR	HR 0.61 95% CI 0.45 - 0.83	4006 patients (3 RCT)	⨁⨁⨁◯	
Overall survival	NR	NR	HR 0.71 95% CI 0.52 - 0.98	4006 patients (3 RCT)	⨁⨁⨁◯	

Summary for Oncology Commission

Patient Overview

- **Diagnosis**: Ductal carcinoma of the left breast (Luminal A)
- **ICD-10 Classification**: C50.9
- **TNM Staging**: pT1c, pN0 (0/11), cM0
- **Stage**: IA
- **Grading**: G2
- **Disease Phase**: Early disease
- **Risk Group**: Low risk
- **Key Biomarkers**:
  - **ER Status**: 3+ (intense nuclear positivity)
  - **PgR Status**: 3+ (intense nuclear positivity)
  - **HER2 Status**: 1+ (weak nuclear positivity, HER2-negative)
  - **Ki-67**: 18%
- **Family History**: Mother with carcinoma of the oral cavity
- **Therapies to Date**:
  - Organ-preserving surgery (quadrantectomy) with axillary lymph node dissection (18.07.2023)
  - Adjuvant radiotherapy and endocrine therapy (decision on 22.08.2023)

Diagnostic Interventions

Recommended Diagnostic Tools

1. **Circulating miRNA Profiling**:
   - Investigated for early detection and differentiation from benign breast conditions.
   - **Quality of Evidence**: Very low due to variability in miRNA expression, limited validation, and small sample sizes.
   - **References**:
     - MiRNAs as potential biomarkers in early breast cancer detection: a systematic review
2. **Breast MRI**:
   - Used for identifying occult multicentric or contralateral breast cancer and assessing local recurrence.
   - **Quality of Evidence**: Very low due to limited sample sizes and potential overdiagnosis.
   - **References**:
     - The impact of sentinel lymph node biopsy and magnetic resonance imaging on important outcomes among patients with ductal carcinoma in situ
3. **Specimen Mammography**:
   - Evaluated for intraoperative margin assessment in breast-conserving surgery.
   - **Quality of Evidence**: Very low due to high heterogeneity in sensitivity and specificity.
   - **References**:
     - Specimen mammography for intraoperative margin assessment in breast conserving surgery: a meta-analysis

analysis

Predictive/Prognostic Biomarkers

Recommended Testing

1. **Ki-67 Labeling Index**:
   - Significant prognostic marker for relapse and overall survival.
   - **Quality of Evidence**: Moderate.
   - **References**:
     - Ki-67 as prognostic marker in early breast cancer: a meta-analysis of published studies involving 12,15 patients
2. **Circulating Tumor DNA (ctDNA)**:
   - Highly predictive of recurrence-free survival and overall survival.
   - **Quality of Evidence**: Low.
   - **References**:
     - Circulating tumor DNA for predicting recurrence in patients with operable breast cancer: a systematic review and meta-analysis
3. **Oncotype DX Genomic Classifier**:
   - Improves risk stratification and prognostic accuracy in hormone receptor-positive early-stage breast cancer.
   - **Quality of Evidence**: Very low.
   - **References**:
     - Systematic review: gene expression profiling assays in early-stage breast cancer
4. **Tumor-Infiltrating Lymphocytes (TILs)**:
   - Associated with recurrence risk and subtype classification.
   - **Quality of Evidence**: Very low.
   - **References**:
     - Tumour-infiltrating lymphocytes in non-invasive breast cancer: A systematic review and meta-analysis

Therapeutic Interventions

Recommended Sequence

1. **Adjuvant Endocrine Therapy**:
   - **Tamoxifen**: 20 mg orally once daily.
   - **Aromatase Inhibitors (e.g., Anastrozole)**: Recommended for postmenopausal women, with switching to anastrozole after 2-3 years of tamoxifen for improved survival outcomes.
   - **Quality of Evidence**: High to very high.
   - **References**:
     - Endocrine Therapy for Ductal Carcinoma In Situ (DCIS) of the Breast with Breast Conserving Surgery (BCS) and Radiotherapy (RT): a Meta-Analysis
     - Effectiveness of switching from adjuvant tamoxifen to anastrozole in postmenopausal women with hormone-sensitive early-stage breast cancer: a meta-analysis
2. **Radiotherapy**:
   - Whole breast irradiation (WBI) following breast-conserving surgery to reduce local recurrence risk.
   - **Quality of Evidence**: High.
   - **References**:
     - Radiotherapy of Breast Cancer-Professional Guideline 1st Central-Eastern European Professional Consensus Statement on Breast Cancer

Summary of Evidence Quality

- **High Quality**: Adjuvant endocrine therapy, radiotherapy.
- **Moderate Quality**: Ki-67 labeling index.
- **Low Quality**: Circulating tumor DNA (ctDNA).
- **Very Low Quality**: Circulating miRNA profiling, Oncotype DX, tumor-infiltrating lymphocytes (TILs), breast MRI, specimen mammography.

Recommendations

1. Prioritize **adjuvant endocrine therapy** (tamoxifen or aromatase inhibitors) and **radiotherapy** as the cornerstone treatment.
2. Incorporate **Ki-67 testing** and **Oncotype DX** for refined prognostic assessment.
3. Consider **ctDNA testing** and **TILs assessment** as supplementary tools for recurrence risk evaluation.
4. Use **circulating miRNA profiling**, **breast MRI**, and **specimen mammography** cautiously, given the very low quality of evidence.

This treatment plan aligns with the patient's low-risk profile and early-stage disease, ensuring optimal outcomes while minimizing unnecessary interventions.

08 / A.P.C.I. Learning & Results | Case 4

- Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) is superior to fine needle aspiration (EUS-FNA) for diagnosing pancreatic masses, with higher diagnostic accuracy and specimen adequacy.

Fine needle biopsy is superior to fine needle aspiration in endoscopic ultrasound guided sampling of pancreatic masses: A meta-analysis of randomized controlled trials. (2018-03-01)

GRADE Table Summary of Findings

Systematic review/MetaAnalysis:
Fine needle biopsy is superior to fine needle aspiration in endoscopic ultrasound guided sampling of pancreatic masses: A meta-analysis of randomized controlled trials.

Patients/Population:
Patients with pancreatic masses revealed by CT, MRI, or EUS

Intervention:
EUS-guided fine needle biopsy (FNB)

Comparator:
EUS-guided fine needle aspiration (FNA)

Outcome	Illustrative Risk		Relative Effect (95% CI)	Number of Participants (Studies)	Overall Quality of Evidence	Comments
	Assumed Risk	Corresponding Risk				
Complications	NR	NR	OR 1.01 95% CI 0.27 - 3.78	1382 patients (10 RCT)	◯◯◯◯	
Technical success	NR	NR	OR 0.13 95% CI 0.02 - 1.07	1382 patients (9 RCT)	◯◯◯◯	
Number of needle passes required for diagnosis	NR	NR	NR	1382 patients (5 RCT)	◯◯◯◯	
Specimen adequacy	NR	NR	OR 1.83 95% CI 1.27 - 2.64	1382 patients (7 RCT)	◯◯◯◯	
Diagnostic accuracy	NR	NR	OR 1.62 95% CI 1.17 - 2.26	1382 patients (10 RCT)	◯◯◯◯	

Oncology Commission Summary: Pancreatic Adenocarcinoma

Patient Overview

- **Patient ID**: №6360/date:16/01/24
- **Age**: 70 years
- **Diagnosis**: Pancreatic adenocarcinoma (ICD-10: C25.0)
- **TNM Staging**: T4N1M1, Stage IV, Grade G2
- **Status**: Active, metastatic disease with liver and lymph node involvement
- **Therapies Performed**: Surgical resection (pancreaticoduodenectomy), systemic chemotherapy (FOLFIRINOX, reduced dose due to hematological toxicity)

Diagnostic Interventions: Practical Sequence

Recommended Sequence:

1. **Contrast-Enhanced CT**: Initial assessment of resectability.
   - **Evidence**: Meta-analysis of 29 studies shows a positive predictive value (PPV) of 0.81.
   - **Limitations**: Retrospective designs, heterogeneity among studies.
   - **Reference**: Contrast-enhanced CT in determining resectability in patients with pancreatic carcinoma
2. **18F-FDG PET/CT**: Prognostic evaluation for event-free survival (EFS) and overall survival (OS).
   - **Evidence**: Hazard ratios for EFS and OS are 1.9 and 1.21, respectively.
   - **Limitations**: Significant heterogeneity (I^2 = 59.8%).
   - **Reference**: Prognostic value of 18F-FDG-PET/CT parameters in patients with pancreatic carcinoma
3. **Serum CA 19-9 Levels**: Preoperative biomarker evaluation.
   - **Evidence**: Limited predictive value for resectability (AUC = 0.794).
   - **Limitations**: Influenced by benign conditions (e.g., jaundice).
   - **Reference**: Preoperative Serum Carbohydrate Antigen 19-9 Levels Cannot Predict the Surgical Resectability of Pancreatic Cancer
4. **Endoscopic Ultrasound-Guided Fine Needle Biopsy (EUS-FNB)**: Tissue sampling.
   - **Evidence**: Superior diagnostic accuracy and specimen adequacy compared to EUS-FNA.
   - **Reference**: Fine needle biopsy is superior to fine needle aspiration in endoscopic ultrasound guided sampling of pancreatic masses
5. **K-ras Mutation Analysis with EUS-FNA**: Differential diagnosis of pancreatic ductal adenocarcinoma (PDAC) vs. pancreatic inflammatory masses (PIM).
   - **Evidence**: Sensitivity 0.9, specificity 0.95.
   - **Reference**: Performance of K-ras mutation analysis plus endoscopic ultrasound-guided fine-needle aspiration for differentiating diagnosis of pancreatic solid mass

Biomarker Testing for Prognostic Evaluation

Recommended Biomarkers:

1. **Liquid Biopsy**: Circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and circulating miRNAs.
   - **Evidence**: Promising for early detection, but very low quality due to small sample sizes and lack of randomization.
   - **Reference**: Advances in the Detection of Pancreatic Cancer Through Liquid Biopsy
2. **Modified Glasgow Prognostic Score (mGPS)**: Prognostic marker for overall survival.
   - **Evidence**: Higher scores indicate worse prognosis (HR = 1.78).
   - **Limitations**: Retrospective designs, heterogeneity.
   - **Reference**: Prognostic and clinical significance of modified glasgow prognostic score in pancreatic cancer
3. **CA19-9 Levels**: Widely used biomarker for prognosis and survival prediction.
   - **Evidence**: Higher levels associated with worse outcomes (HR = 1.7).
   - **Limitations**: Observational designs, inconsistencies.
   - **Reference**: Prognostic Role of Carbohydrate Antigen 19 to 9 in Predicting Survival of Patients With Pancreatic Cancer
4. **Platelet-to-Lymphocyte Ratio (PLR)**: Prognostic marker for overall survival.
   - **Evidence**: Elevated PLR associated with worse outcomes (HR = 1.22).
   - **Limitations**: Retrospective designs, publication bias.
   - **Reference**: Prognostic role of platelet to lymphocyte ratio in pancreatic cancers

Evidence Quality Modifier

Finding	QoE Modifier	Comment
Risk of Bias	-2	High risk of performance bias due to lack of blinding of endos

Starting QoE: 3 (QualityOfEvidence.HIGH). CI width > 0.8 => quality of evidence -1 CI contains 1 => quality of evidence -2 Current QoE: 0. After application of negative modifiers: 0. After application of positive modifiers: 0.

CLOSE

Therapeutic Interventions: Practical Sequence

Recommended Sequence:

1. **First-Line Therapy**:
   - **FOLFIRINOX**: Preferred for patients with good performance status (ECOG PS 0-1).
     - **Evidence**: Superior overall survival compared to gemcitabine-based therapies.
     - **Reference**: Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline
   - **Gemcitabine + Nab-Paclitaxel**: Alternative for patients with ECOG PS 2 or comorbidities.
     - **Evidence**: Effective for patients unable to tolerate FOLFIRINOX.
     - **Reference**: Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline
2. **Second-Line Therapy**:
   - **Liposomal Irinotecan + Fluorouracil + Leucovorin**: For progression after first-line gemcitabine-based therapy.
     - **Evidence**: Viable option with limited data.
     - **Reference**: Metastatic Pancreatic Cancer: ASCO Clinical Practice Guideline Update

Summary of Evidence Quality

- **Diagnostic Interventions**: Evidence quality ranges from very low to moderate, with significant limitations due to heterogeneity, retrospective designs, and small sample sizes.
- **Biomarker Testing**: Evidence quality is predominantly very low, emphasizing the need for further validation in larger, randomized studies.
- **Therapeutic Interventions**: High-quality evidence supports the use of FOLFIRINOX and gemcitabine + nab-paclitaxel as first-line therapies. Second-line options require further robust data.

This summary provides a structured approach to the diagnosis, prognostic evaluation, and treatment of metastatic pancreatic adenocarcinoma, tailored to the patient's clinical profile.

09 / Expected Outcomes and Potential Limitations

Expected Outcomes

- **Insights into the personalized performance** of the large language model (LLM) within the A.P.C.I. system in real-world clinical settings.
- **GRADE-based evidence** supporting optimized clinical workflows and enhanced data-driven insights guiding decision-making for multidisciplinary tumour boards.
- **Data-driven insights** informing further development and global implementation of **standalone LLM-based multidisciplinary clinical decisions support system** in oncology, by overcoming language and geographical barriers.

Potential Limitations

- **Biases associated with the retrospective study design**, which may limit control over confounding variables.
- **Heterogeneity of electronic health record (EHR) data** across different centers, **and clinical practices (SOPs)** potentially impacting result quality.
- **Incomplete patient data**, particularly regarding long-term outcomes, which may affect the robustness of conclusions.

© Shemha Health, 2025

10 / Conclusions

By integrating large language model (Gen-AI) with the GRADE approach, this study evaluates the potential of A.P.C.I. to revolutionize oncology decision-making processes by enhancing diagnostic accuracy, personalizing treatment pathways, and optimizing the efficiency of multidisciplinary teams.

The findings will play a crucial role in clinical validation, scientific dissemination, and fostering strategic collaboration with key stakeholders. This will drive the adoption of AI-enhanced GRADE methodology within the Comprehensive Cancer Infrastructure (CCI), ensuring global scalability and impact in precision oncology.

© Shemha Health, 2025

W / www.propa.health
E / ivaylo.petrov@shemhahealth.com
T / +359 885 995 353

LinkedIn / Shemha Health
Facebook / PrOPA by Shemha Health
Instagram / propa.health

MedTech World 2024, AI in Health Awards

HITLAB Breakthrough Alliance Challenge 2024 FINALIST | NYC, US

Forbes Bulgaria 2024 Start-up & Social Innovation Awards