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PODCAST

ESMO Podcast on upper gastrointestinal cancers—highlights in biliary and pancreatic cancers from ASCO 2025

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In this episode of the European Society for Medical Oncology (ESMO) podcast series on upper gastrointestinal cancers, host Dr Jeroen Dekervel (UZ Leuven, Belgium) is joined by Dr Arndt Vogel (Princess Margaret Cancer Center, Toronto and Hannover, Germany) and Dr Florian Castet (Vall d'Hebron University Hospital, Barcelona) to critically discuss key trial results in pancreatic and biliary tract cancers presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2025.

The discussion begins with the CASSANDRA trial, a randomized phase III study comparing neoadjuvant chemotherapy regimens in resectable and borderline resectable pancreatic ductal adenocarcinoma (PDAC). The experimental PAXG regimen (nab-paclitaxel, gemcitabine, cisplatin, and capecitabine) showed a significant improvement in event-free survival compared with modified FOLFIRINOX. However, both guests noted caution due to the composite primary endpoint—including carbohydrate antigen 19-9 (CA19-9) elevation—and the absence of confirmed overall survival benefit, suggesting the regimen may be considered for very fit patients but not yet as standard of care.

The PANOVA-3 trial explored the use of tumor-treating fields (TTFs) in combination with chemotherapy for locally advanced unresectable PDAC. TTFs modestly improved overall survival, but progression-free survival remained unchanged. The panel highlighted uncertainties related to placebo effect, low compliance, and staging inconsistencies, but acknowledged the innovation and potential of this novel approach in a disease with limited options.

In metastatic PDAC, the Elraglusib (Actuate 1801) phase II trial added a glycogen synthase kinase 3 beta (GSK-3β) inhibitor to chemotherapy and demonstrated a survival benefit. While the results are encouraging, concerns were raised about the high toxicity (notably visual disturbances and fatigue), low performance of the control arm, and the need for better patient selection—possibly via biomarkers—before moving to phase III.

The conversation then shifts to biliary tract cancer (BTC). The GAIN trial examined neoadjuvant chemotherapy before surgery in resectable BTC and showed improved survival and R0 (no tumor at the margin) resection rates, but the trial's early closure and imbalances between arms limit interpretation. The Indian POLCA-GB trial evaluated chemoradiotherapy in locally advanced gallbladder cancer and demonstrated a significant survival benefit, reviving interest in the role of radiotherapy in BTC.

Overall, the panel welcomes the encouraging signals across PDAC and BTC trials while emphasizing the importance of rigorous study design, longer follow-up, and confirmatory data before shifting clinical practice.

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