A randomized non-comparative phase II study of maintenance OSE2101 vaccine alone or in combination with nivolumab (nivo), or FOLFIRI after induction with FOLFIRINOX in patients (Pts) with advanced pancreatic ductal adenocarcinoma (PDAC): first interim results of the TEDOPAM GERCOR D17-01 PRODIGE 63 STUDY

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Abstract # 4148

BACKGROUND

- Results of immune therapies in PDAC have so far been disappointing
- PDAC displays a **challenging tumor microenvironment** for cytotoxic T cells and **innovative combination immunotherapies** are needed
- OSE2101 (Tedopi®) is a **multiple neoepitope vaccine** composed of 10 synthetic peptides (targeting CEA, HER2-Neu, p53, MAGE2, MAGE3 that are frequently found **overexpressed in PDAC**) with **HLA-A2 restricted presentation**
- **This study aims to assess the efficacy and safety of OSE2101 ± anti-PD1 nivo in Pts with advanced PDAC after FOLFIRINOX induction chemotherapy (CTx)**

RESULTS

Baseline demographics

Out of 162 screened Pts, 66 (41.9%) were HLA-A2 positive

	Arm A FOLFIRI N=9	Arm B OSE2101 N=10	Arm C OSE2101 + nivo N=10
Men, n (%)	5 (55.6)	4 (40.0)	6 (60.0)
Median age, interquartile range (IQR)	59, 51-63	63.5, 54-71	66, 59-73
Metastatic stage, n (%)	8 (88.9)	8 (80.0)	7 (70.0)
ECOG Performance Status 0 (PS), n (%)	4 (44.4)	5 (50.0)	7 (70.0)
Median CA19-9, IQR	129 (35-1008)	202 (5-1072)	59 (33-655)
Partial response to induction FOLFIRINOX, n (%)	5 (55.6)	4 (40.0)	5 (50.0)

Activity

- With a median follow-up was 23 months (95% CI 15.4-25.6), **M12-OS rate** was 44% in Arm A, 40% in Arm B, and 30% in Arm C
- Median PFS was 6.3 (1.8-NA) in Arm A, 2.7 (0.9-3.8) in Arm B, and 2.2 (1.6-4.0) in Arm C
- Objective responses (partial responses) during maintenance were observed in n=1 (11%) in Arm A, n=1 (10%) in Arm B, n=0 (0%) in Arm C

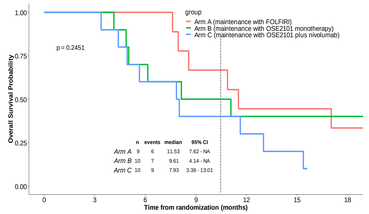


Fig 1. Overall survival according to study arm

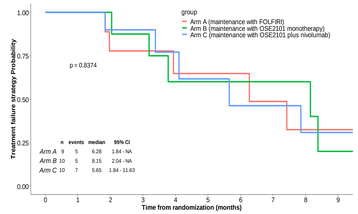


Fig 2. Time to failure of the strategy according to study arm

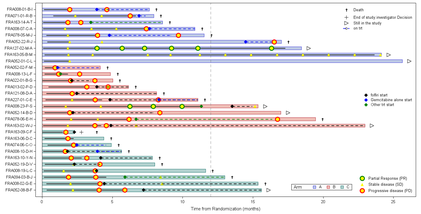


Fig 3. Swimmer plot for radiological evaluation according to study arm

MATERIAL AND METHODS

Study Design

- ✓ Advanced PDAC
- ✓ **HLA-A2 genotype (blood)**
- ✓ ECOG PS 0-1
- ✓ No progression after 8 cycles of FOLFIRINOX

Non-comparative phase II
N=156

Reference Arm – Arm A
FOLFIRI (*n=52*)

FOLFIRINOX 8 cycles → R (1:1:1)

Experimental Arms
Arm B
OSE2101 (*n=52*) → FOLFIRI reintroduction at disease progression

Arm C
OSE2101 + nivo (*n=52*) → FOLFIRI reintroduction at disease progression

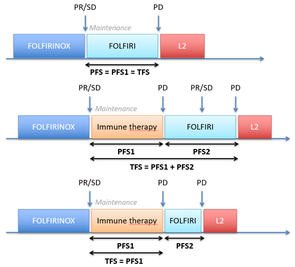
Until progression, death, or unacceptable toxicity

Stratification:
- Center,
- Tumor stage (locally advanced vs metastatic),
- Best response to induction CTx (SD vs PR/CR)

OSE2101: subcutaneous injection on D1 Q3W/6 doses then Q8W until M12 then Q12W up to M24
Nivo: 360 mg IV on D1 Q3W x 6 then 480 mg Q4W up to M24

Endpoints

- **Primary endpoint**: Overall survival (OS) at 12 months (M12-OS, Fleming 2-stage design, H0 ≤ 25% / H1 ≥ 50%; α = 2.5%, β = 10%)
- **Secondary objectives**: Progression-free survival (PFS), time to failure of strategy (TFS – see below), objective response rate (ORR), safety, health-related quality of life (HRQoL)



L2: second line of treatment

Safety

- A total of 10 SAEs was reported: n=2 (22%) Arm A, n=3 (30%) Arm B, n=5 (50%) Arm C
- No OSE2101-related toxicity of grade ≥ 3 were observed in Arm B
- One grade 3 cytokine-release syndrome (OSE2101-related) and two tumor flares (nivo-related) leading to death were observed in Arm C
- **Following the occurrence of the latest, an Independent Data Monitoring Committee (IDMC) recommended to continue FOLFIRI as backbone in experimental Arm B and stop Arm C**

Translational Research *(ongoing)*

- To explore biomarkers and pharmacodynamics effects of OSE2101:
  (i) tumor tissue (initial formalin-fixed paraffin-embedded biopsy and optional re-biopsy at inclusion), RNA-sequencing (cancer and stromal signatures), mutation burden, mismatch repair status, immune infiltrates, cancer-associated fibroblast subtypes, intratumor microbiota
  (ii) blood (before and on-treatment): cytokine panel, peripheral blood mononuclear cell phenotyping, vaccine-antigen specific T-cells, T cell receptor repertoire, and extracellular vesicles

CONCLUSIONS

- Maintenance with OSE2101 monotherapy showed **a favorable safety profile** and **encouraging TFS** warranting further evaluation
- OSE2101 + nivo was associated with poorer outcomes leading to termination of Arm C
- Following the IDMC recommendation, **the study is ongoing with the new design (maintenance FOLFIRI vs. FOLFIRI + OSE2101)**
- **ClinicalTrials registration: NCT03806309**

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