# Promising Phase 1b/2 Results with TG4001, in Combination with Avelumab, in HPV16-Positive Cancers

November 2020

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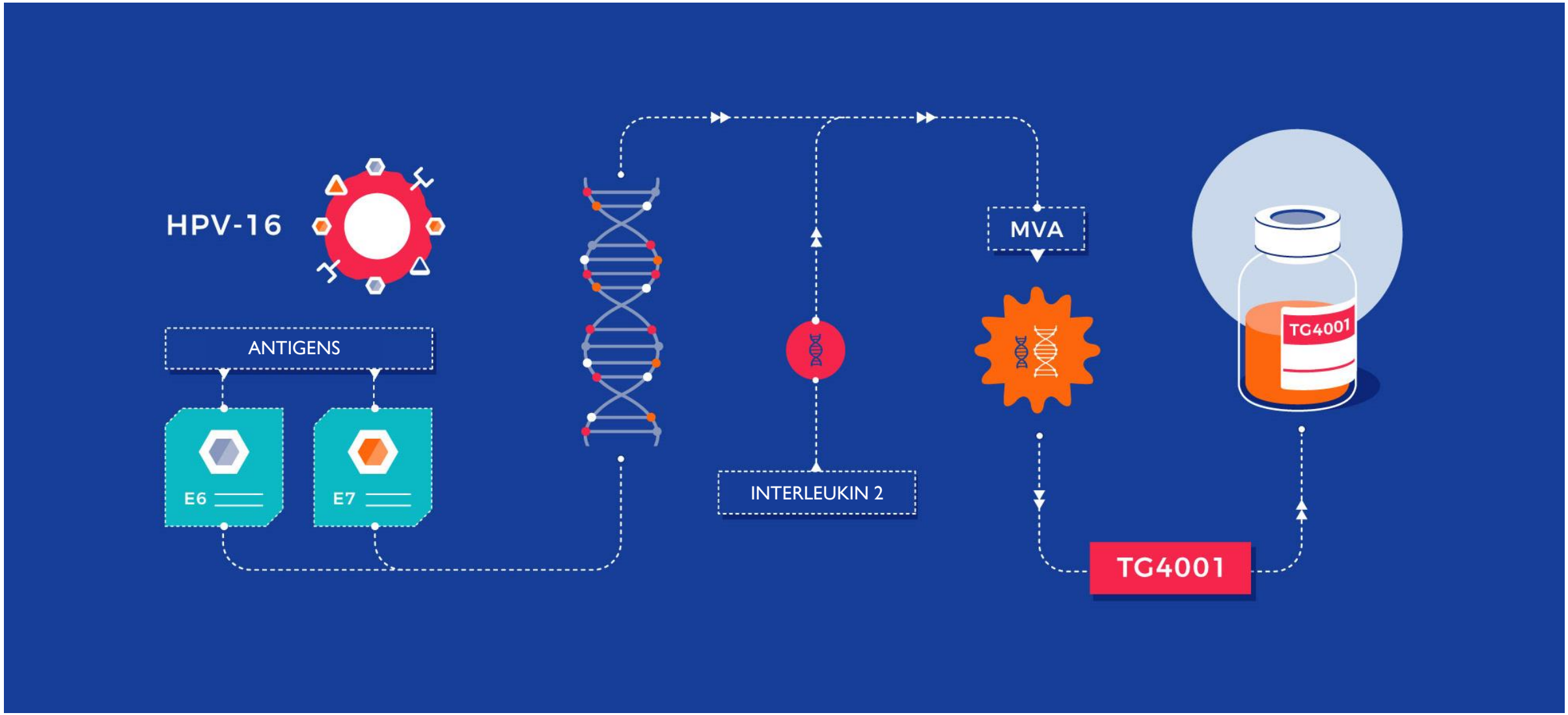
# **TG4001** | Therapeutic vaccine targeting HPV-positive cancers



# **TG4001** | Therapeutic vaccine targeting HPV-positive cancers

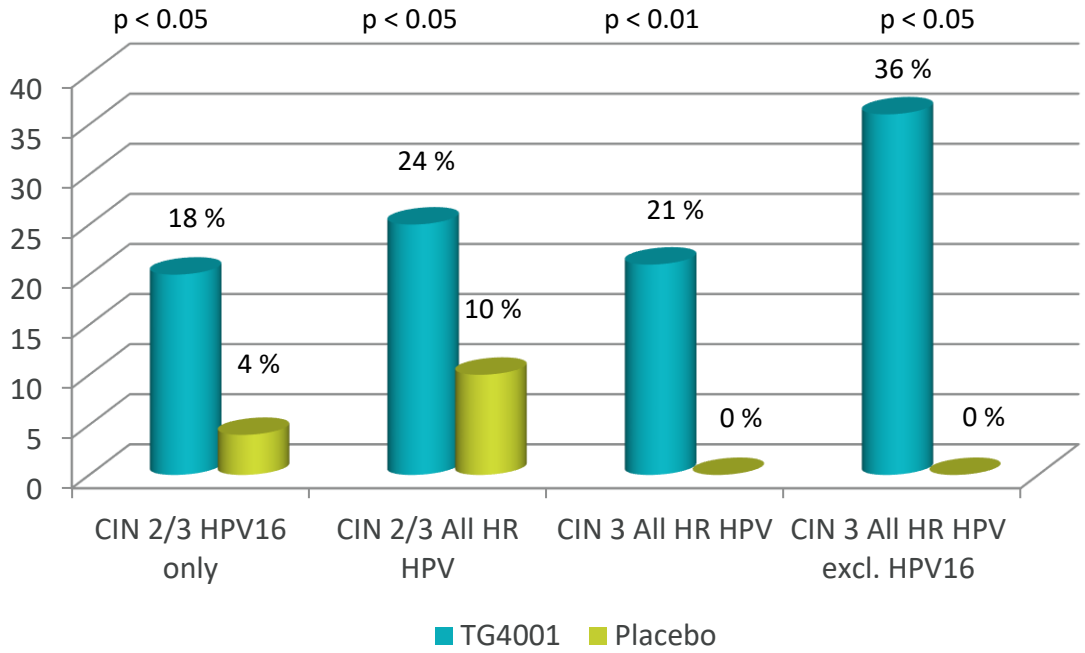
➲ Designed to boost the patient's immune system against the tumor

## Strong data for TG4001 in the clinic (1-2)

- ✓ **Strong and specific response against tumor cells carrying HPV16 E6 & E7 antigens**
- ✓ **Stimulates the infection-clearing activity** of the immune system
- ✓ **Long-lasting responses**
- ✓ **Good combination candidate** thanks to established **safety profile**

## Complete resolution at 6 months (%) (1)

*TG4001 single-agent vs placebo*



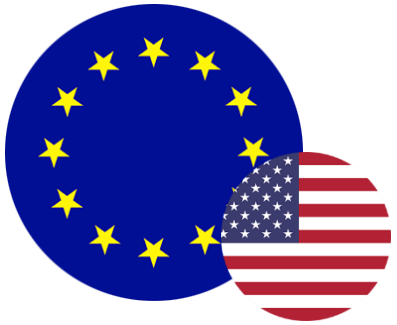

**Strong rationale for testing TG4001 in advanced stage HPV-positive cancers**

# Significant opportunity for TG4001 in HPV16 positive cancers

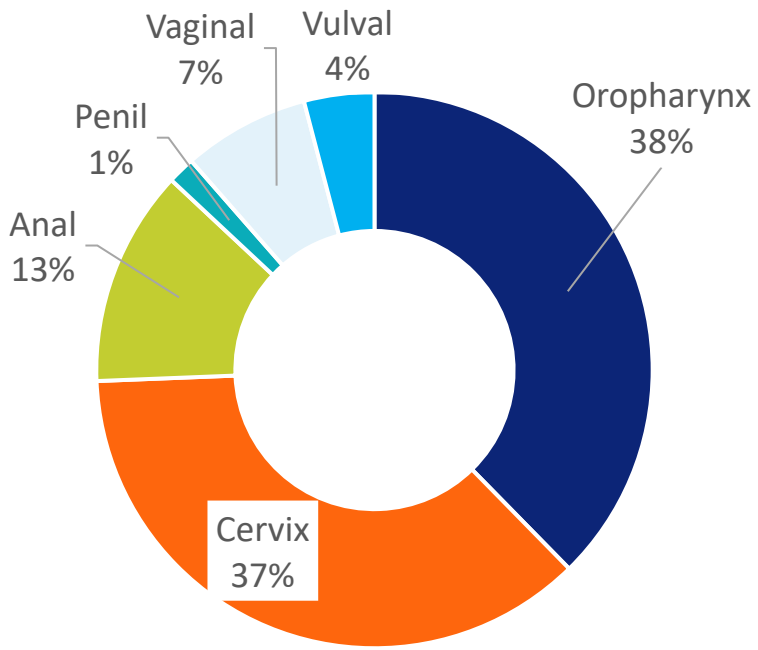
**Incidence of HPV16 positive cancers**
*Stage 4 (metastatic 2L)*

**~ 25,000 new patients**
per year

**75% EU28**



**25% USA**




**Increasing proportion** of oro-pharyngeal and anogenital cancers caused by HPV, mostly HPV16

**Chronic infection with HPV** leads to cancerous lesions after 10-20 years

Sources: see notes 3 to 10 on slide 24

# A Phase 1b/2 trial assessing TG4001 and avelumab in advanced HPV16-positive cancers

# No specific treatment for HPV16-positive cancers

**Current treatments do not address the etiology (viral origin) of the disease**

## Current standards of care include:

- In first line of treatment:
  - Head & neck cancers: checkpoint blockers (EU + USA)
  - Other indications: diversity of treatments, including chemotherapy
- In second line of treatment:
  - Head & neck (EU + USA) and cervix cancers (USA): checkpoint blockers
  - Other indications: diversity of treatments, including chemotherapy

# HPV16 associated cancer patients need better treatment options

| | KN040 [11] N = 495 (1:1)<br>Phase 3<br>Head and Neck | | CM 141 [12] N =361 (2:1)<br>Phase 3<br>Head and Neck | | JAVELIN [13]<br>Phase 1b<br>Head and Neck | Nivolumab NCI9673 [14]<br>Phase 2<br>Anal | KN028 + KN158 [15] (pooled analysis) Phase 1b (KN028) and Phase 2 (KN158)<br>Anal | CARACAS [16]<br>Phase 2<br>Anal | | KN158 [17]<br>Phase 2<br>Cervical | CM 358 [18]<br>Phase 2<br>Cervical, vaginal vulvar |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Treatment<br>N | Pembrolizumab<br>N = 247 | SOC*<br>N = 248 | Nivolumab<br>N = 240 | SOC*<br>N = 121 | Avelumab<br>N = 153 | Nivolumab<br>N = 37 | Pembrolizumab<br>N = 137 | Avelumab<br>N = 30 | Avelumab + Cetuximab<br>N = 30 | Pembrolizumab<br>N = 98 | Nivolumab<br>N = 19 cervical<br>N = 5 vaginal/ vulvar |
| **ORR** | 14.6%<br>(36) | 10.1%<br>(25) | 13.3%<br>(32) | 5.8%<br>(7) | 13.1%<br>(20) | 24%<br>(9) | 10.9% | 10%<br>(3) | 17%<br>(5) | 12.2%<br>(12) | 26.3%<br>20.0% |
| **Med PFS** | 2.1 m | 2.3 m | 2.0 m | 2.3 m | 1.8 m | 4.1 m | 2.1 m | 2.1 m | 3.9 m | 2.1 m | 5.1 m |
| **Med OS** | 8.4 m | 6.9 m | 7.5 m | 5.1 m | 8.0 m | 11.5 m | 11.7 m | 10.8 m | 6.8 m | 9.4 m | 21.9 m |

**ORR is around 10–15% , median PFS is around 2 months and median OS is less than 11 months**

* SOC: methotrexate, docetaxel, cetuximab

# **TG4001** | Phase 1b/2 in combination with Avelumab in HPV+ cancers

## Patients

- Metastatic or refractory/recurrent HPV16+ cancer
- Up to two prior lines of systemic therapy for the management of metastatic or recurrent disease
- **No previous exposure to cancer immunotherapies**
- ECOG PS 0 or 1
- Adequate hematological, hepatic and renal function

## Enrollment

- 34 evaluable patients

## Data cutoff date

- Mid-August 2020

## Principal Investigator

- Pr Christophe Le Tourneau, Institut Curie

## Treatment regimen

**TG4001: $5x10^7$ pfu – administered SC**

- Weekly for 6 weeks, then every 2 weeks to month 6, and every 12 weeks

**Avelumab: 10mg/kg – administered IV**

- Every 2 weeks

**Collaboration with**

MERCK Pfizer institutCurie

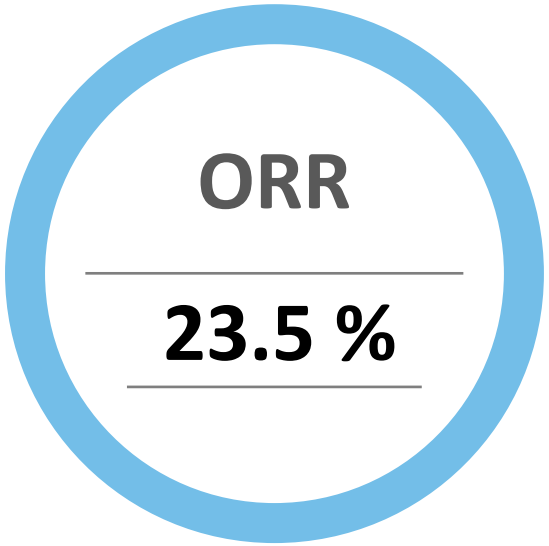
# Patient characteristics

| | Patients without liver metastases (N=23) | Patients with liver metastases (N=11) | Overall (N=34) |
|---|---|---|---|
| **Age (years)** | | | |
| Mean | 61.6 | 52.9 | 58.8 |
| Range | 28 - 78 | 34 – 79 | 28 - 79 |
| **Gender** | | | |
| Female | 14 | 8 | 22 (64.7%) |
| Male | 9 | 3 | 12 (35.3%) |
| **Performance Status (ECOG)** | | | |
| 0 | 7 | 7 | 14 (41.2%) |
| 1 | 16 | 4 | 20 (58.8%) |
| **Primary tumor** | | | |
| Anal | 7 | 8 | 15 (44.1%) |
| Cervical | 5 | 1 | 6 (17.6%) |
| Oropharyngeal | 8 | 0 | 8 (23.5%) |
| Vaginal | 2 | 2 | 4 (11.8%) |
| Vulvar | 1 | 0 | 1 (2.9%) |
| **Number of organs Involved** | | | |
| 1 | 9 | 3 | 12 (35.3%) |
| 2 | 10 | 3 | 13 (38.2%) |
| 3 | 4 | 5 | 9 (26.5%) |
| **Number of CT lines for R/M disease** | | | |
| 0 | 4 | 0 | 4 (11.8%) |
| 1 | 14 | 5 | 19 (55.9%) |
| 2 | 5 | 6 | 11 (32.4%) |

# TG4001 + avelumab demonstrate anti-tumor activity

## Population

**34 evaluable patients**




**1 complete response**

*Patient with anal cancer and peritoneal extension that all disappeared – still followed in the trial*

**7 partial responses**

- Responses were observed in **all primary tumor types** and **across all lines of prior therapy**

**Compares favorably to ICIs in monotherapy**

# Encouraging results in patients without liver metastasis

## Population

**23 patients without liver metastasis**

*vs patients with liver metastasis (n=11)*

**ORR**

**34.8 %**

*vs 0%*

**m PFS**

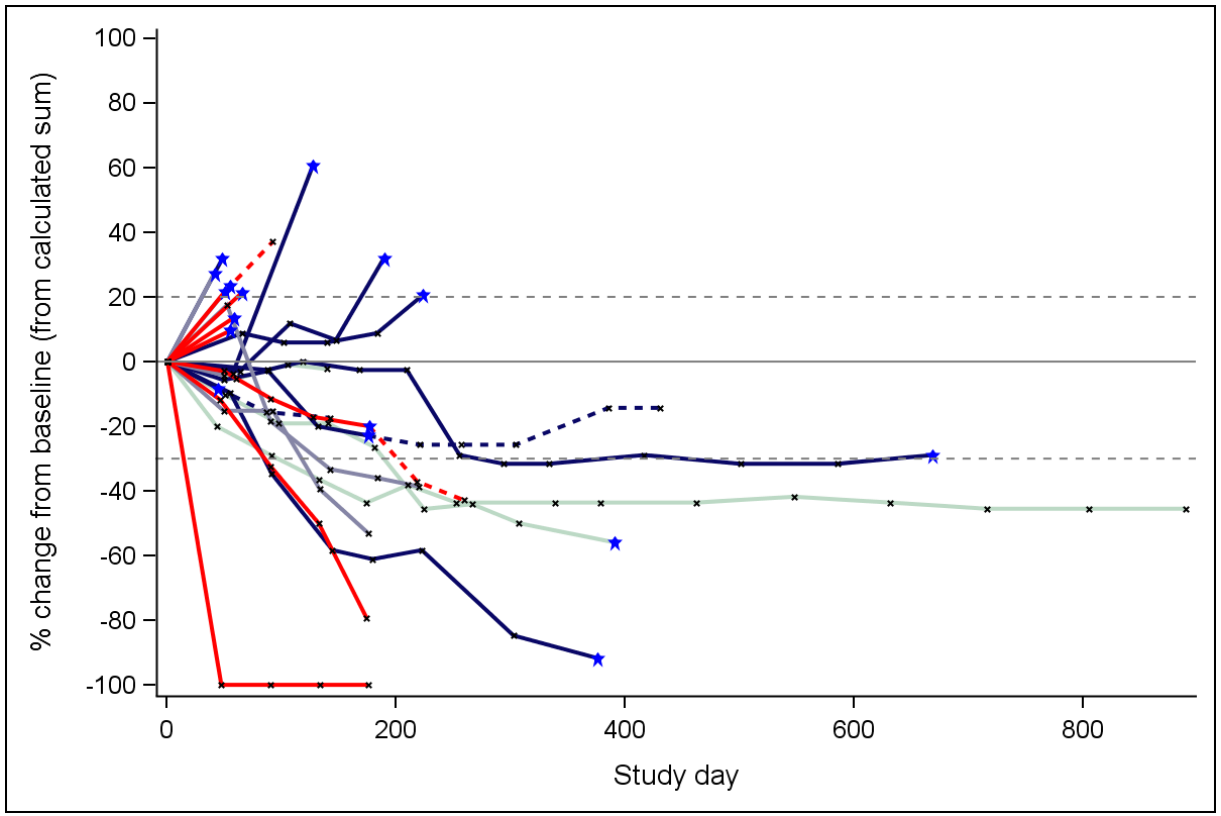
**5.6 months**

*vs 1.4 month*

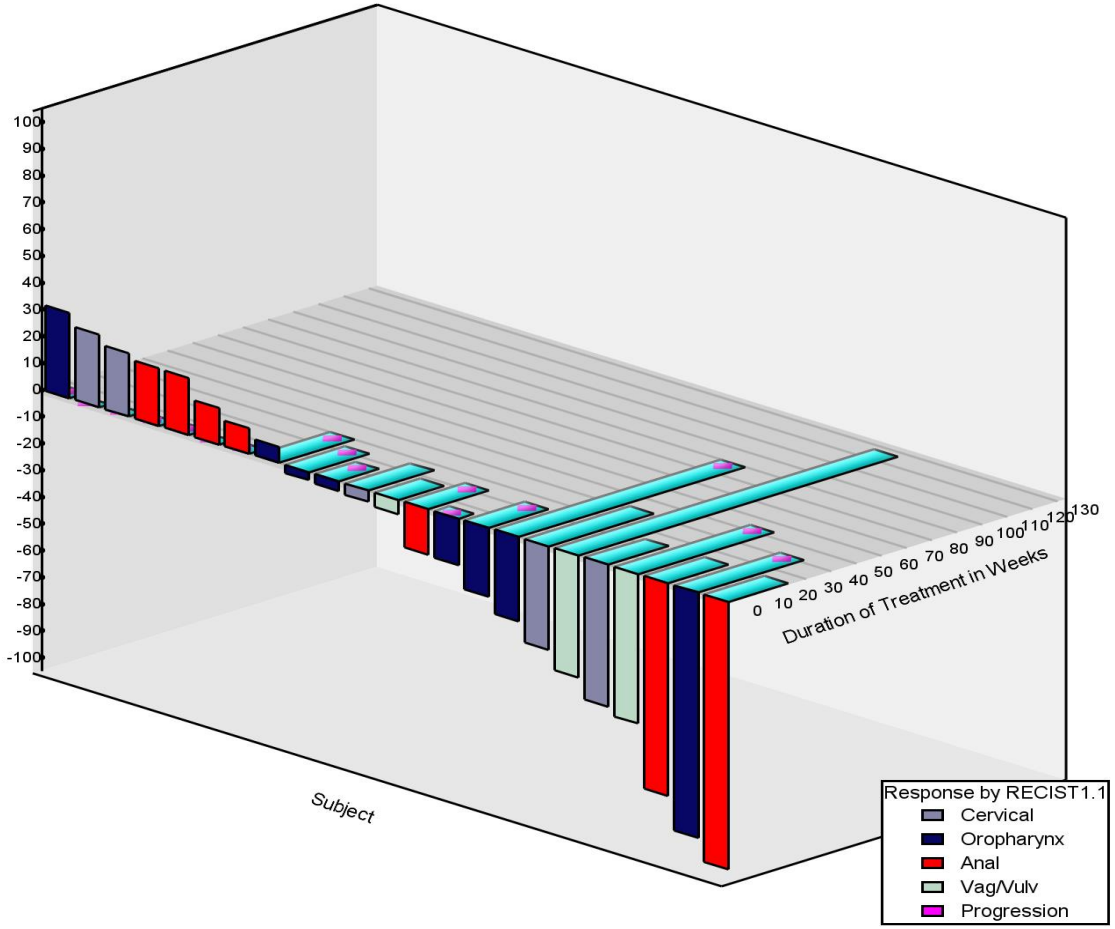
**Compares favorably to ICIs in monotherapy and competitive landscape**

# Long-lasting responses – Patients follow up ongoing

**Evolution of tumor size in patients without liver metastases**



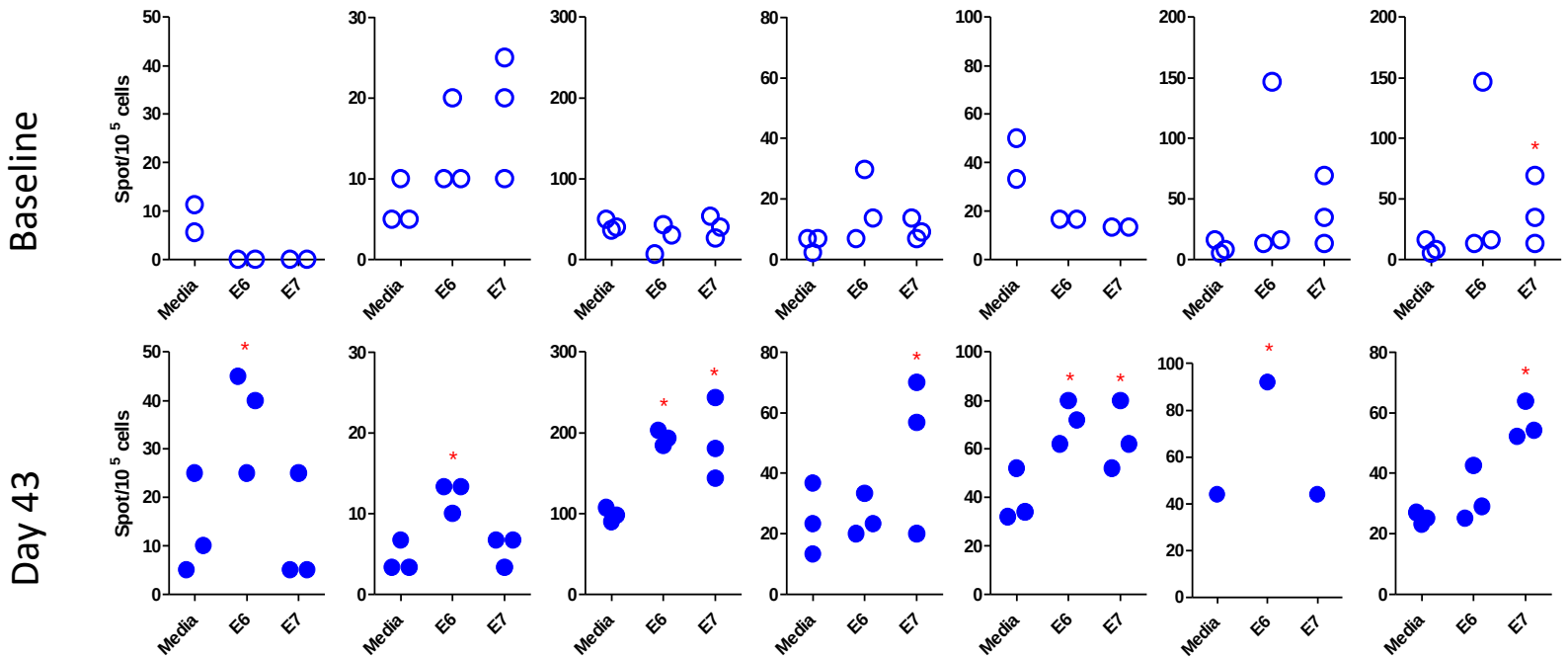

**Best percentage change from baseline / Duration of treatment in patients without liver metastases**



# TG4001 elicits specific T-cell response against HPV16 E6 and E7

**Patients with a detected response against target antigens**

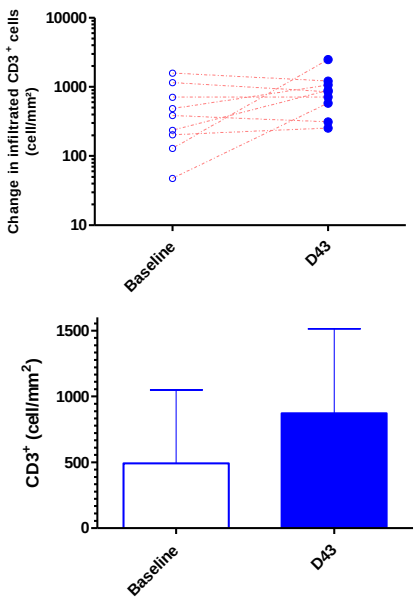
*(Ex vivo ELISPOT response against E6 and E7)*



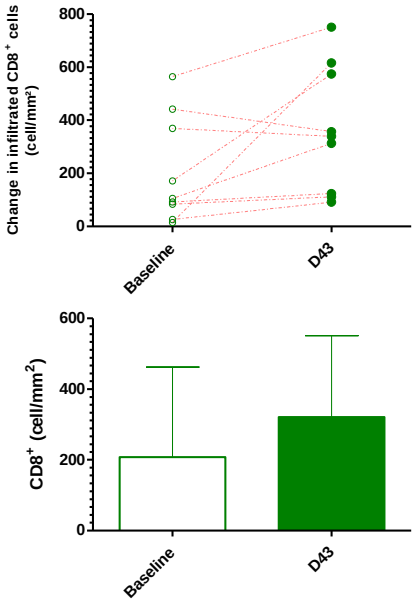

- At baseline, no patient showed a specific response against E6 and E7
- 7/11 patients evaluable for ELISPOT show specific T-cell responses against HPV16 E6 and E7 after vaccination with TG4001
- Results support durable control of the disease

# Treatment shifts « cold » tumor into « hot » tumor

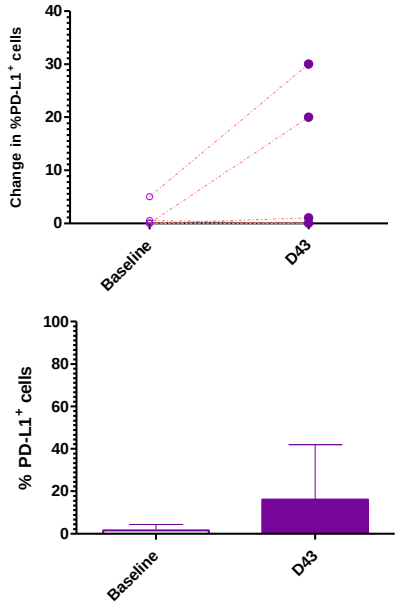
**CD3+ infiltrate**



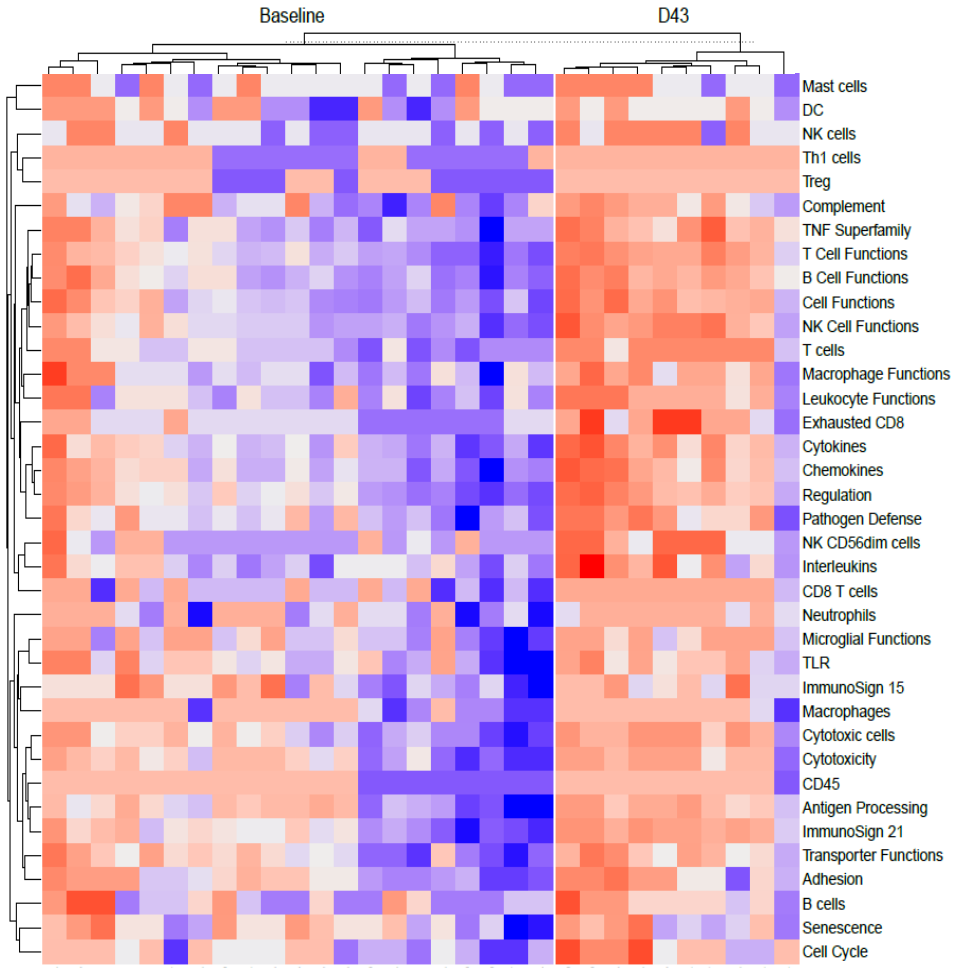

**CD8+ infiltrate**




**PD-L1 expression**

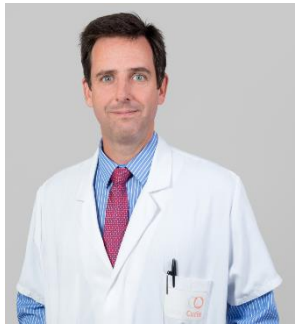



**Gene expression**



# KOLs support further development of TG4001

*We have seen very encouraging efficacy results in this hard-to-treat patient population, as well as a satisfying safety profile. I believe this combination regimen has the opportunity to provide real hope for patients with HPV16 related cancers.*



Prof. Christophe Le Tourneau, MD
Principal Investigator
Head of the Department of Drug Development and Innovation (D3i)@ Institut Curie

## PARTICIPATING CENTERS (Phase 1b/2 trial)

- INSTITUT CURIE • PARIS
- CENTRE LÉON BÉRARD • LYON
- IUCT ONCOPOLE • TOULOUSE
- HÔPITAL PASTEUR • COLMAR
- ICO CENTRE RENÉ GAUDUCHEAU • NANTES
- ICO CENTRE PAUL PAPIN • ANGERS
- APHM HÔPITAL DE LA TIMONE • MARSEILLE

# An upcoming trial to further validate the potential of TG4001

## Further validation in larger population

- Combination with immune checkpoint inhibitor
- HPV16-positive cancers
- Randomized, controlled
- Europe and US
- Regulatory filing before year end

**Strategy is to retain rights to increase shareholder value**

# Detailed references and resources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