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

November 2020

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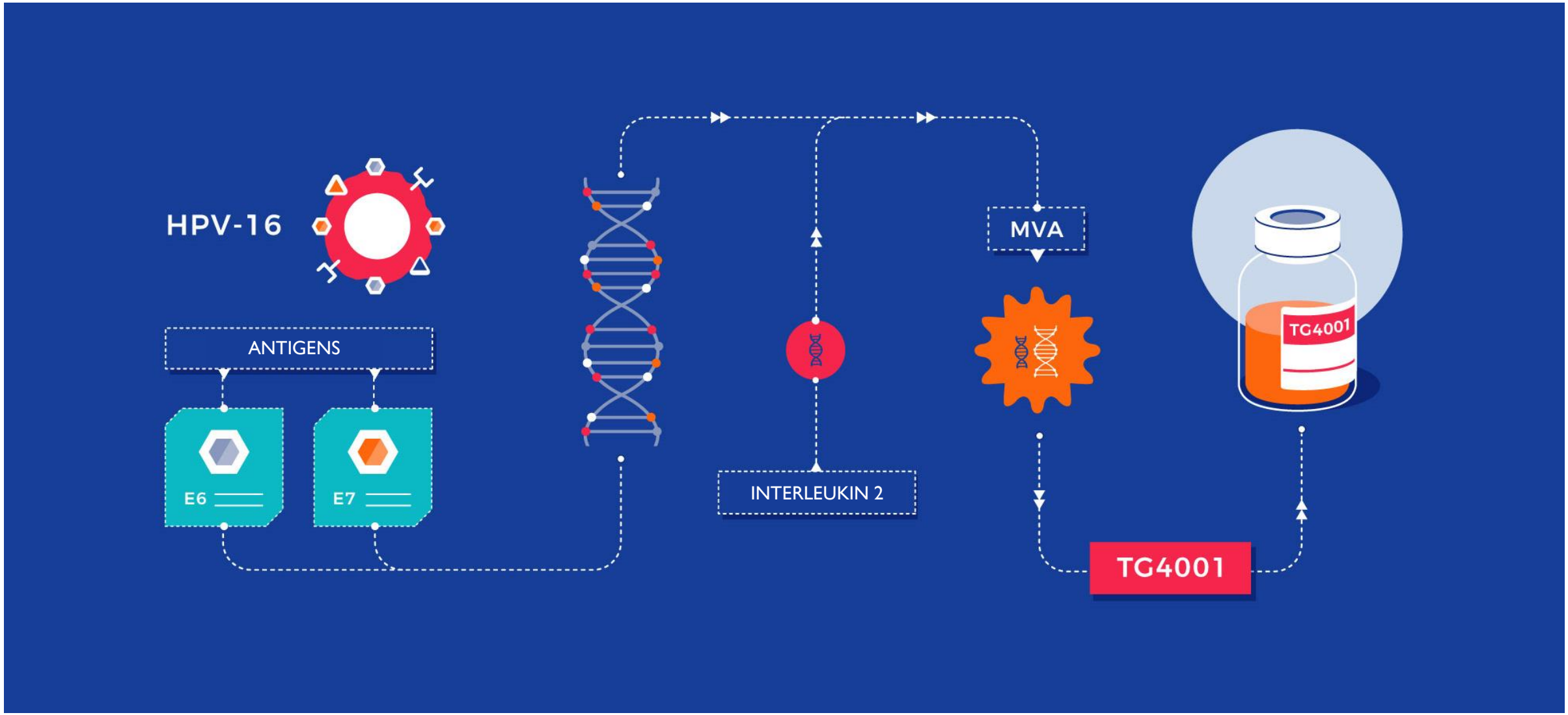
TG4001 | Therapeutic vaccine targeting HPV-positive cancers



TG4001 | Therapeutic vaccine targeting HPV-positive cancers

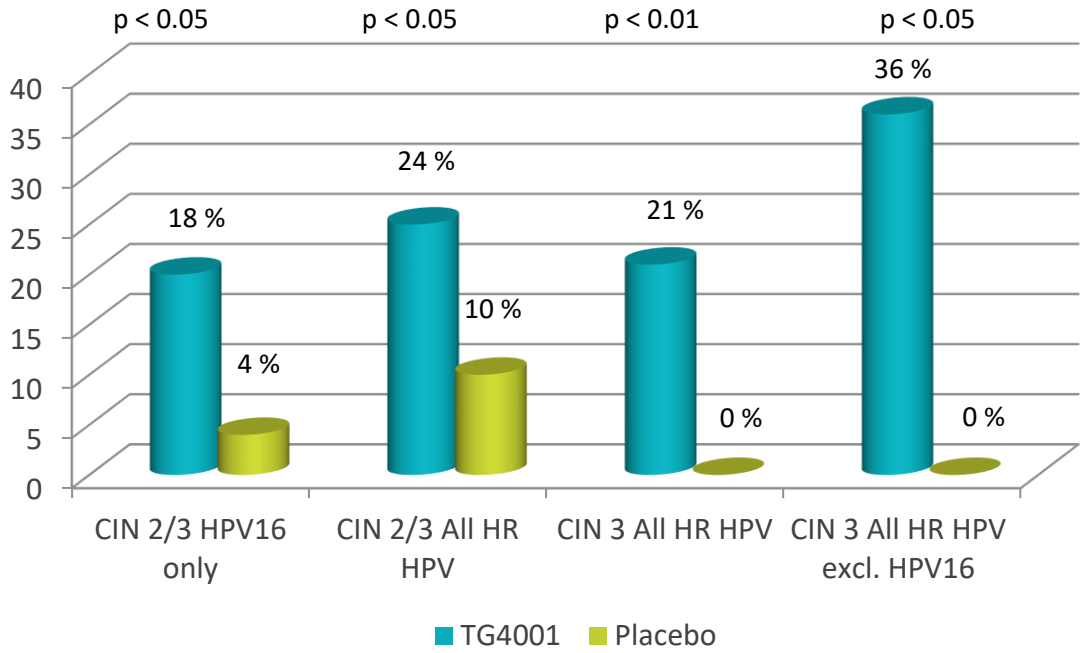
➲ Designed to boost the patient's immune system against the tumor

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



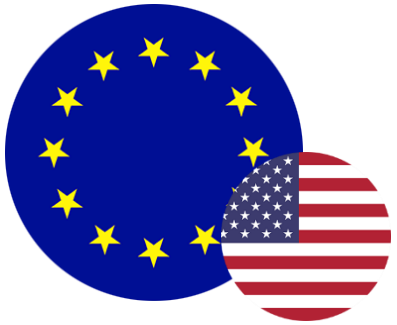
Strong rationale for testing TG4001 in advanced stage HPV-positive cancers

Significant opportunity for TG4001 in HPV16 positive cancers

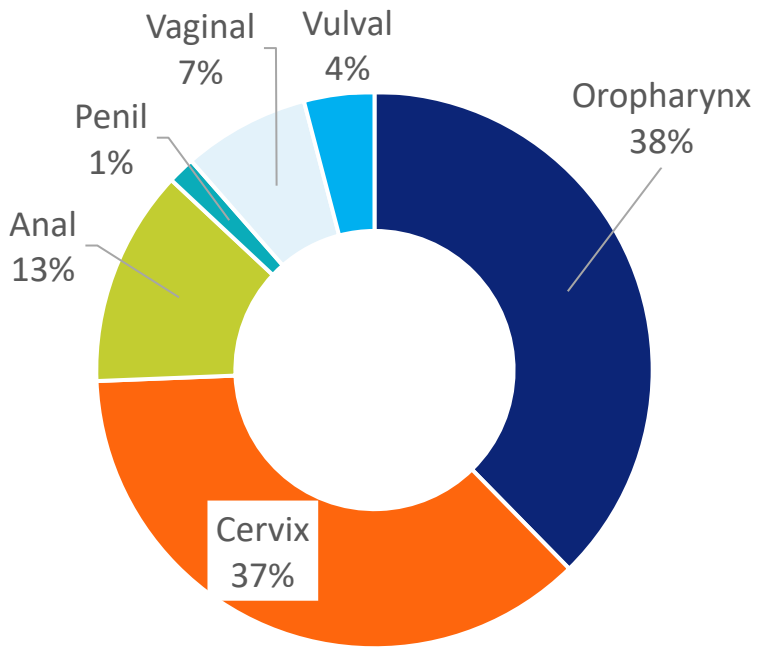
Incidence of HPV16 positive cancers
Stage 4 (metastatic 2L)

~ 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) Phase 3 Head and Neck		CM 141 [12] N =361 (2:1) Phase 3 Head and Neck		JAVELIN [13] Phase 1b Head and Neck	Nivolumab NCI9673 [14] Phase 2 Anal	KN028 + KN158 [15] (pooled analysis) Phase 1b (KN028) and Phase 2 (KN158) Anal	CARACAS [16] Phase 2 Anal		KN158 [17] Phase 2 Cervical	CM 358 [18] Phase 2 Cervical, vaginal vulvar
Treatment N	Pembrolizumab N = 247	SOC* N = 248	Nivolumab N = 240	SOC* N = 121	Avelumab N = 153	Nivolumab N = 37	Pembrolizumab N = 137	Avelumab N = 30	Avelumab + Cetuximab N = 30	Pembrolizumab N = 98	Nivolumab N = 19 cervical N = 5 vaginal/ vulvar
ORR	14.6% (36)	10.1% (25)	13.3% (32)	5.8% (7)	13.1% (20)	24% (9)	10.9%	10% (3)	17% (5)	12.2% (12)	26.3% 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

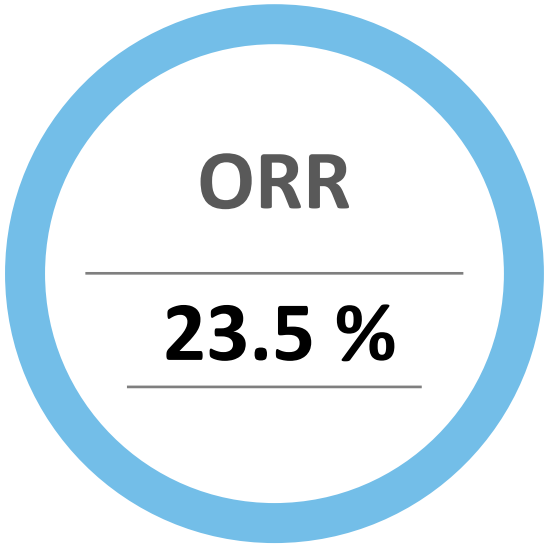
Patient characteristics

	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

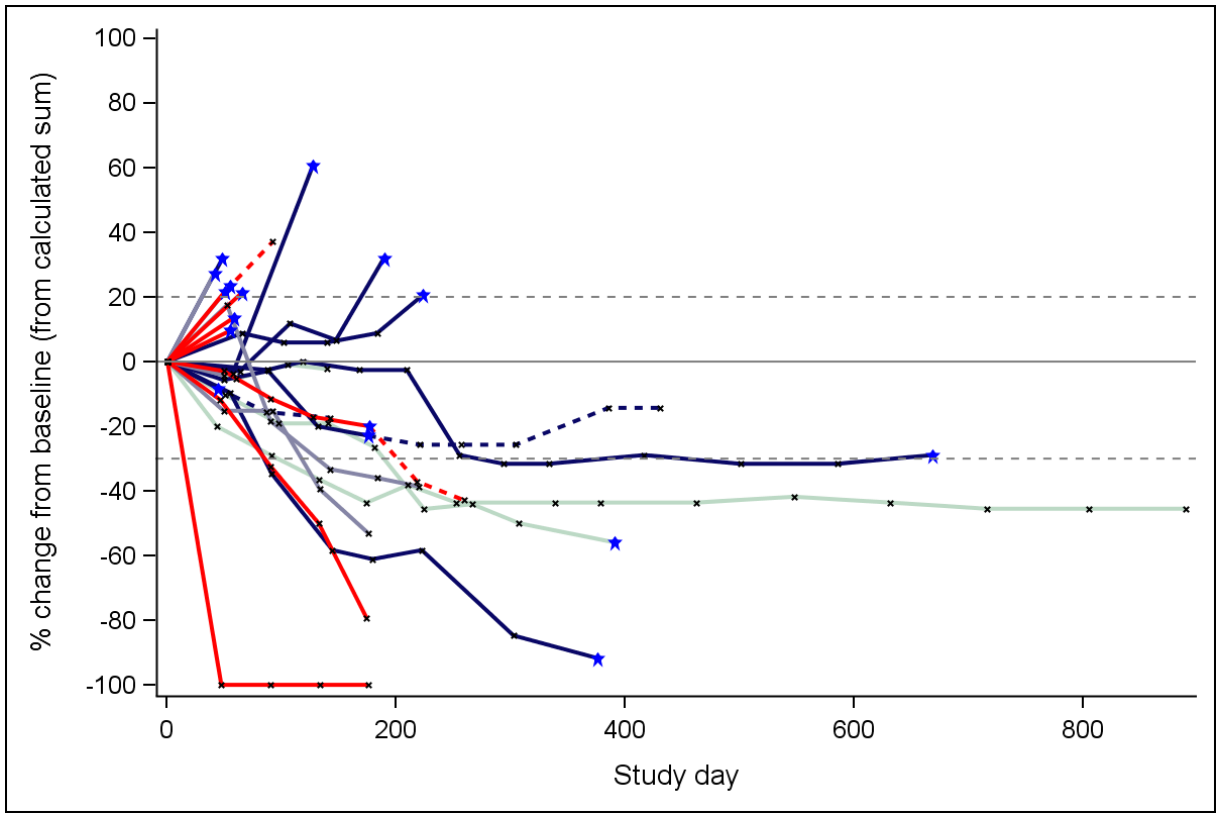
5.6 months

vs 1.4 month

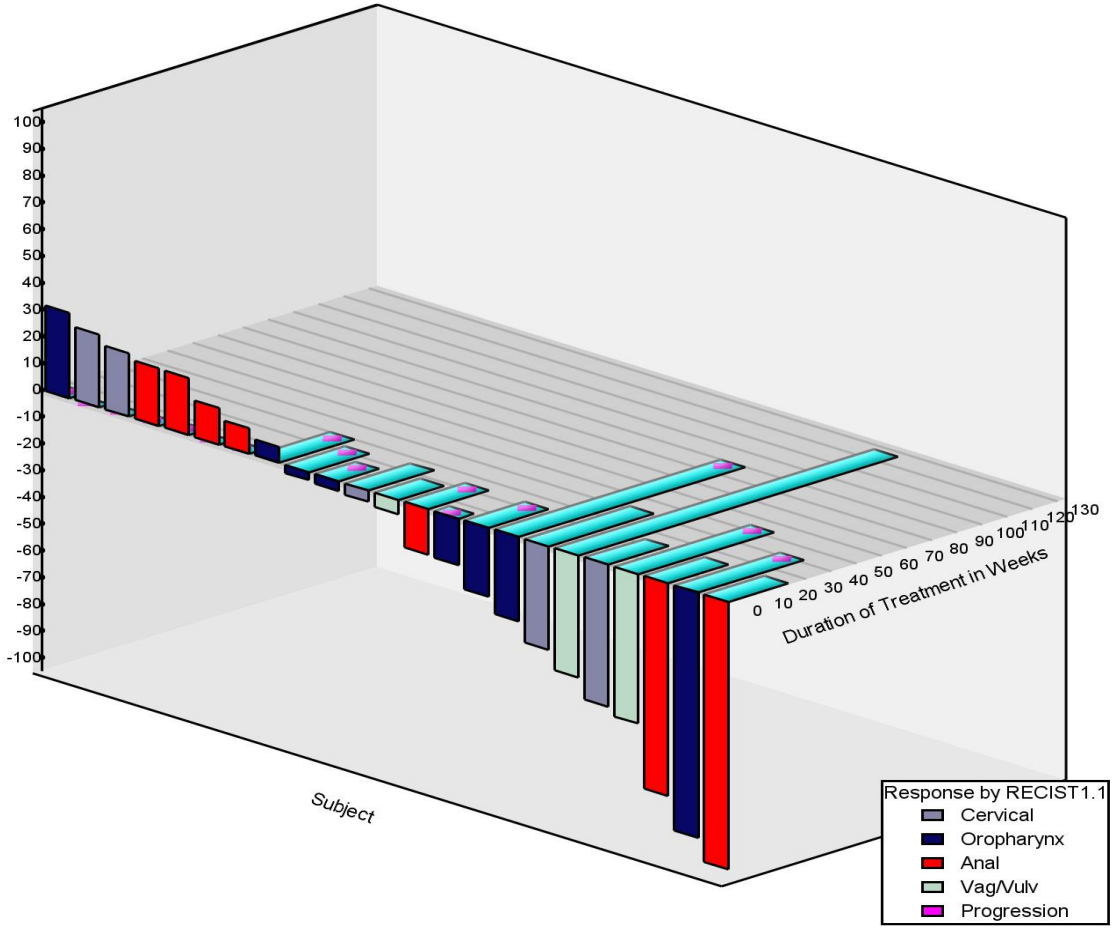
Compares favorably to ICIs in monotherapy and competitive landscape

Long-lasting responses – Patients follow up ongoing

Evolution of tumor size in patients without liver metastases



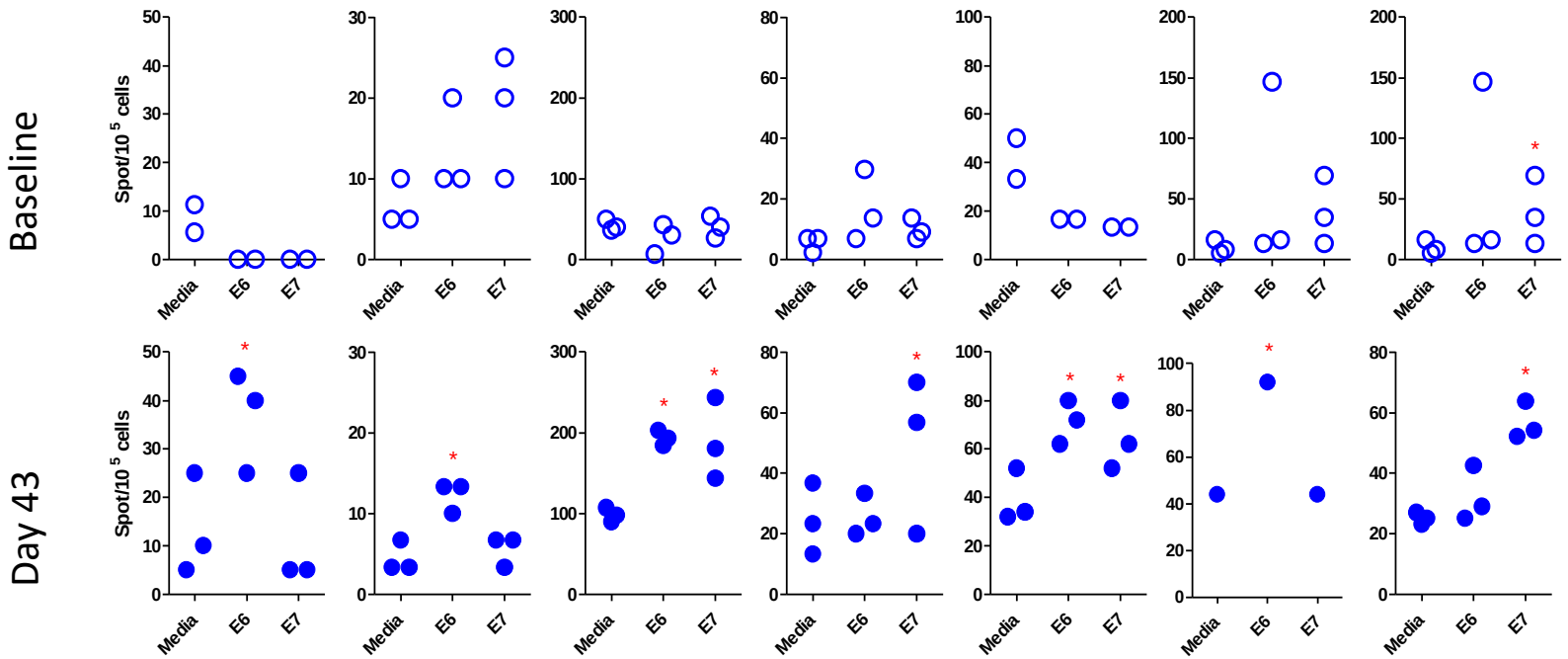
Best percentage change from baseline / Duration of treatment in patients without liver metastases



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

Patients with a detected response against target antigens

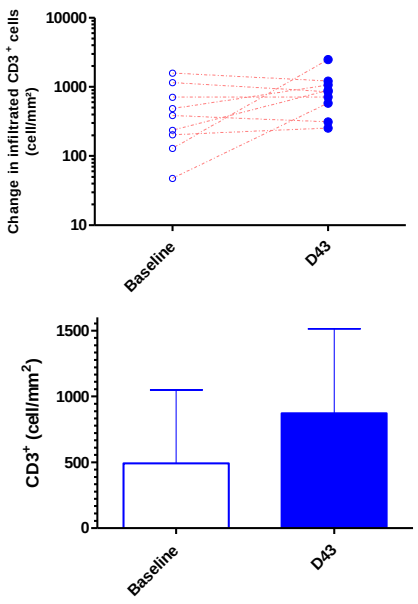
(Ex vivo ELISPOT response against E6 and E7)



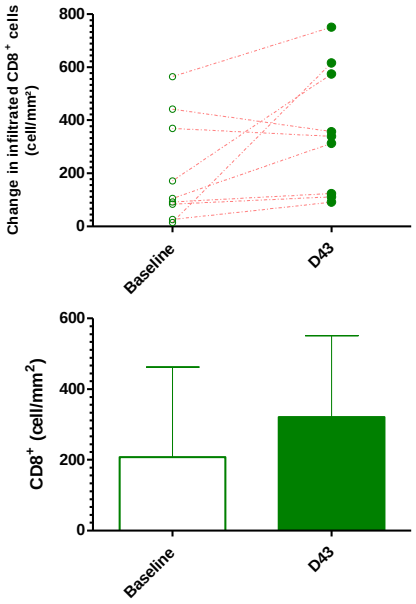
- At baseline, no patient showed a specific response against E6 and E7
- 7/11 patients evaluable for ELISPOT show specific T-cell responses against HPV16 E6 and E7 after vaccination with TG4001
- Results support durable control of the disease

Treatment shifts « cold » tumor into « hot » tumor

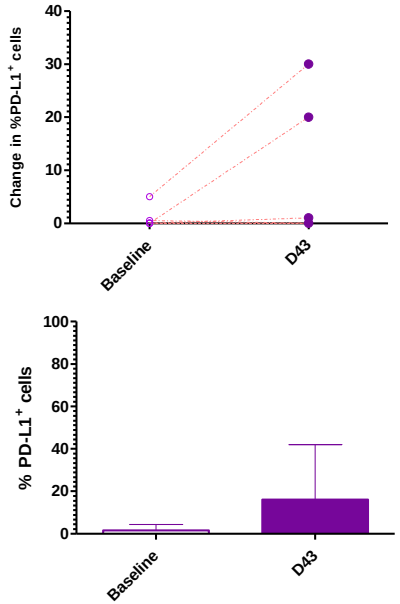
CD3+ infiltrate



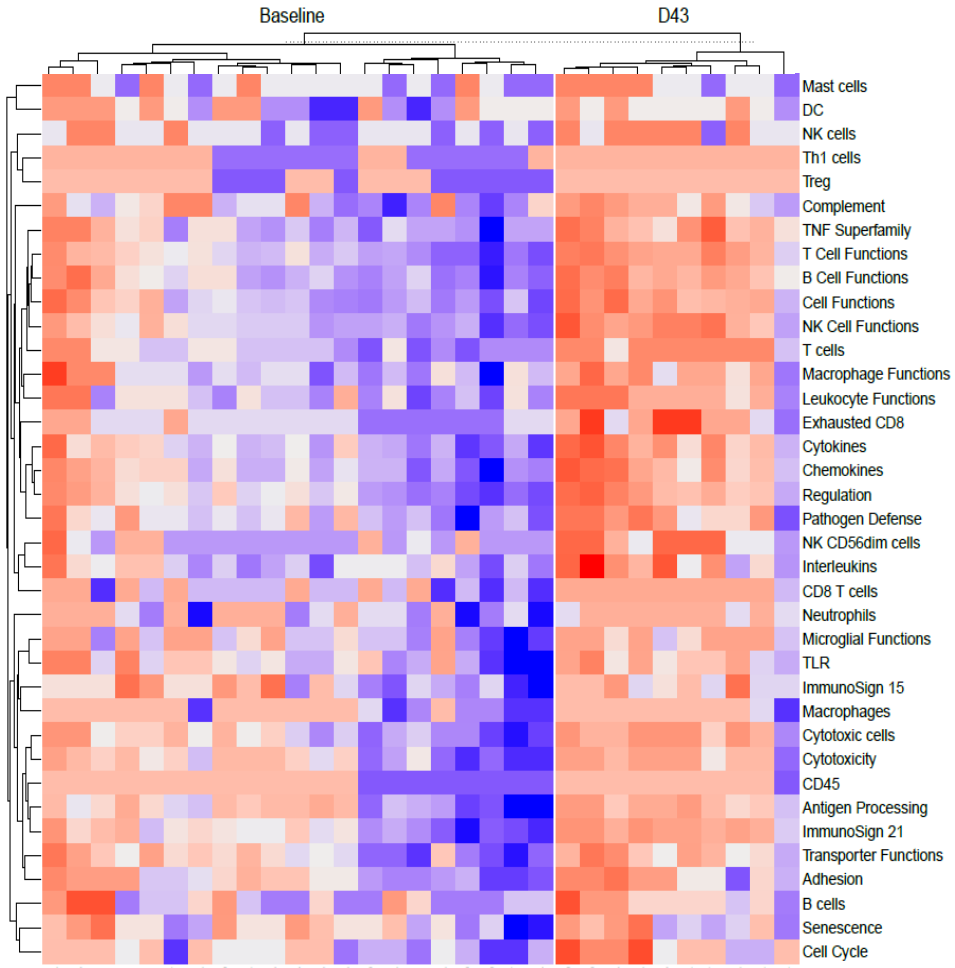
CD8+ infiltrate



PD-L1 expression

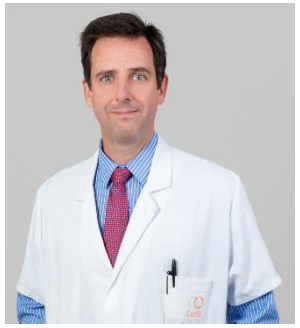


Gene expression



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.



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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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