



Promising Phase 1b Results with
TG4001, in combination with Avelumab,
in HPV16-Positive Cancers
Presented at ESMO

Today's call



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Disclaimer

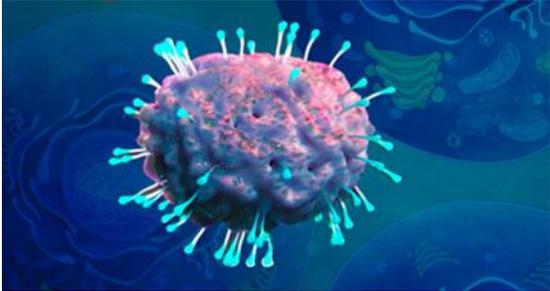
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TG4001 + Avelumab in HPV16+ cancers - Key takeaways

- Landmark data - First PoC efficacy data for the combination of a MVA-based therapeutic vaccine with an immune checkpoint inhibitor (ICI)
 - **3 patients with durable responses**
 - **50% of the 6 patients treated with the Phase 2 dose**
 - **Very challenging population (PFS < 5 months) – heavily pre-treated – 100% distant metastases**
 - **Phase 1b data further confirm safety and biological activity of the combination regimen**
- Phase 2 ongoing since October 2018 - Interim analysis planned for 1H 2020

TG4001 | Therapeutic vaccine targeting HPV-positive cancers



Optimized virus

- Attenuated MVA

Transgenes

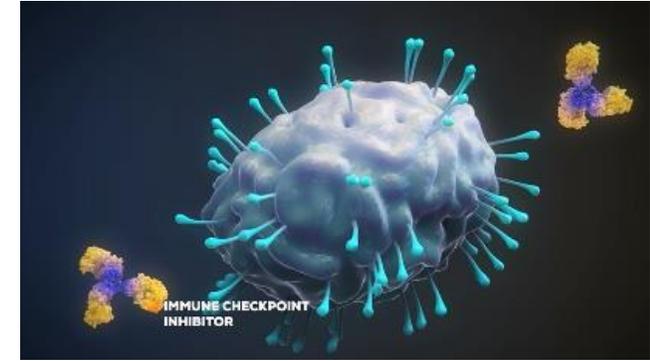
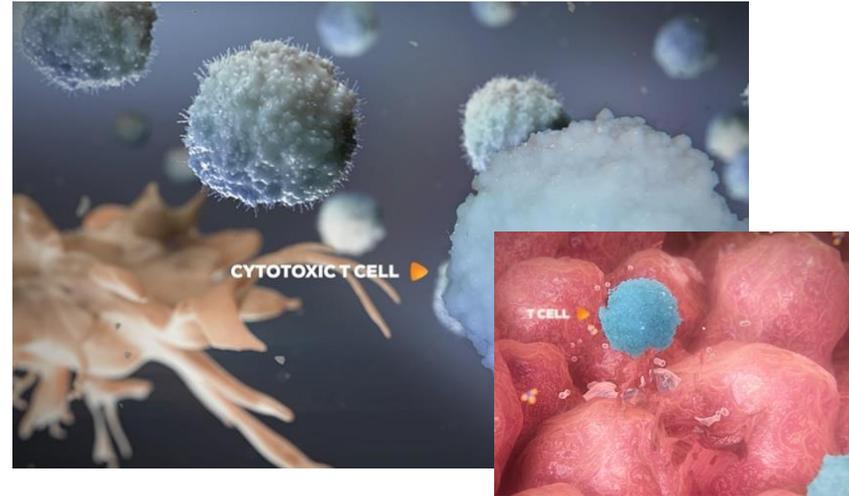
- HPV16 E6&7 antigens
- IL2



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

- 1 Targeted response against tumor cells carrying the HPV16 E6 & E7 antigens
- 2 Stimulate the infection-clearing activity of the immune system through interleukin 2
- 3 Good combination candidate thanks to established safety profile

TG4001 | Stimulates a safe and specific immune response



- Antigen (HPV16 E6 & E7) expression
- Leading to maturation of Antigen Presenting Cell (APC)
- Mature APCs present HPV16 E6 & E7 antigens to naive T-cells

- T-cells get activated , multiply and reach the blood stream
- Activated T-cells infiltrate the tumor, recognize and kill HPV16 E6 & E7 tumor cells

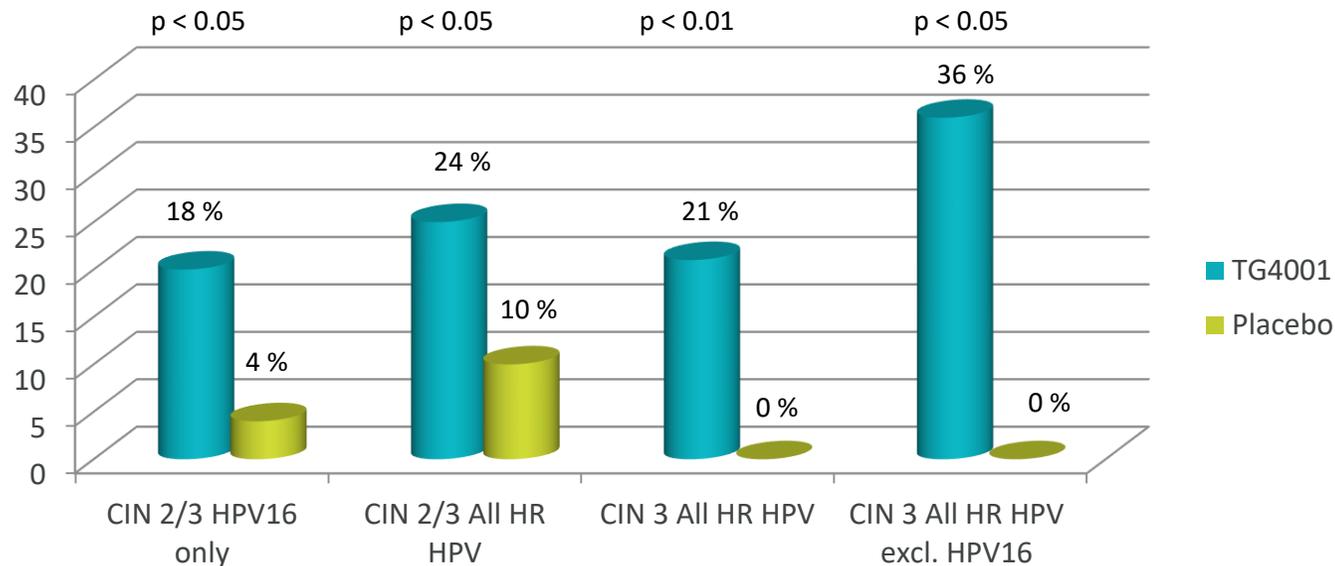
Potential additional benefit when combined **with immune checkpoint inhibitors (ICIs)**

TG4001 | Positive Phase 2b in HPV-associated CIN 2/3

Monotherapy delivered statistically significant curative activity

- ✓ Single agent TG4001 is active and able to address HPV-related carcinomas
- ✓ Data represent a strong POC of active immunotherapy

Complete resolution
at 6 months (%)



THE LANCET
Oncology

“This is the first time that we have seen such a high level of HPV and grade 2–3 CIN clearance with a therapeutic vaccine,” notes Harper. Peter Sasieni (King's College London, London, UK) welcomed the findings. “The results are scientifically important,” he said. ***“They open up the possibility of exploring whether the vaccine can be applied to other HPV-associated cancers and anal or vulvar lesions, which are much harder to treat.”***

[Editorial](#) (April 2019)

TG4001 | Targeting HPV-positive malignancies

- ✓ **Efficacy demonstrated*** in patients with high grade CIN associated with HPV16
- ✓ **Clinical experience in more than 300 patients**, demonstrating good safety profile. Injection site reactions were the most common adverse events
- ✓ **Strong rationale for testing TG4001 in advanced stage HPV-positive cancers**
 - ➔ High unmet medical need

HPV16 associated cancer patients need better treatment options

	KN040 N = 495 (1:1)		CM 141 N = 361 (2:1)		Nivolumab NCI9673 Phase 2 Anal	KN028 Phase 1b Anal – PDL1 ≥1%	KN158 Phase 2 Cervical
	Phase 3 Head and neck		Phase 3 Head and neck				
Treatment N	Pembrolizumab N = 247	SOC* N = 248	Nivolumab N = 240	SOC* N = 121	Nivolumab N = 37	Pembrolizumab N=25	Pembrolizumab N=98
ORR	36 (14.6%)	25 (10.1%)	32 (13.3%)	7 (5.8%)	9 (24%)	4 (17%)	12 (12.2%)
Med OS	8.4 m	6.9 m	7.5 m	5.1 m	11.5 m	9.3 m	9.4 m
Med PFS	2.1 m	2.3 m	2.0 m	2.3 m	4.1 m	3.0 m	2.1 m

* SOC: methotrexate, docetaxel, cetuximab

Median PFS between 2 and 4 months and median OS between 7 and 11 months

Significant opportunity for TG4001 in HPV16 positive cancers

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

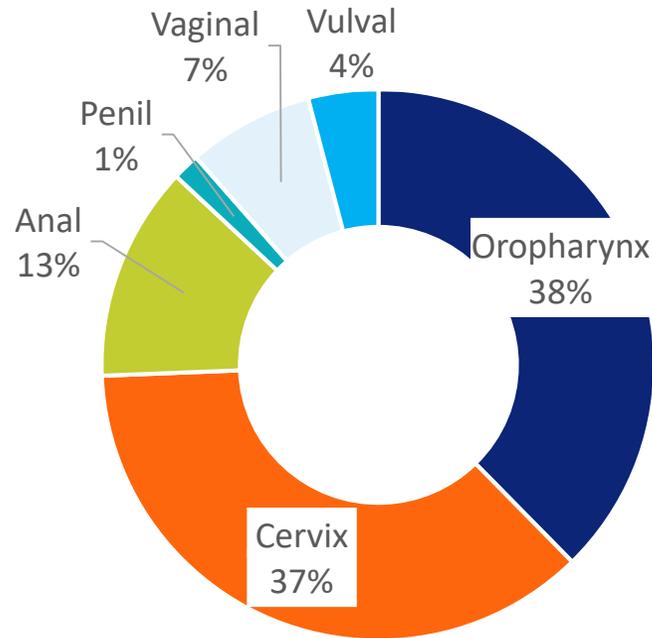


~ 25,000 new patients
per year

75% EU28



25% USA



Increasing proportion of oropharyngeal and anogenital cancers caused by HPV, mostly HPV16



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



Based on recent data, TG4001 could be priced at **€50,000 in the EU** and **\$100,000 in the USA**

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

➔ Phase 1b efficacy data presented @ESMO 2019

In collaboration with

MERCK

Pfizer

institutCurie

Principal Investigator

- Pr Christophe Le Tourneau, Institut Curie

Key Eligibility Criteria

- **Histologically or cytologically documented metastatic / recurrent HPV16+ cancer** (central)
- **Up to two prior lines of systemic chemotherapy for the management of metastatic or recurrent disease**
- ECOG PS 0 or 1
- Agreeing to undergo a pre- and post-treatment tumor biopsies
- At least 1 measurable lesion by CT scan
- Adequate hematological, hepatic and renal function
- **No previous exposure to cancer immunotherapies**

Primary Endpoint

Phase Ib: Safety of the combination [*R/M HPV16+ advanced malignancies*]

Phase II: ORR (RECIST 1.1)

[*R/M HPV16+ advanced malignancies including oropharyngeal SCCHN*]

Secondary Endpoints

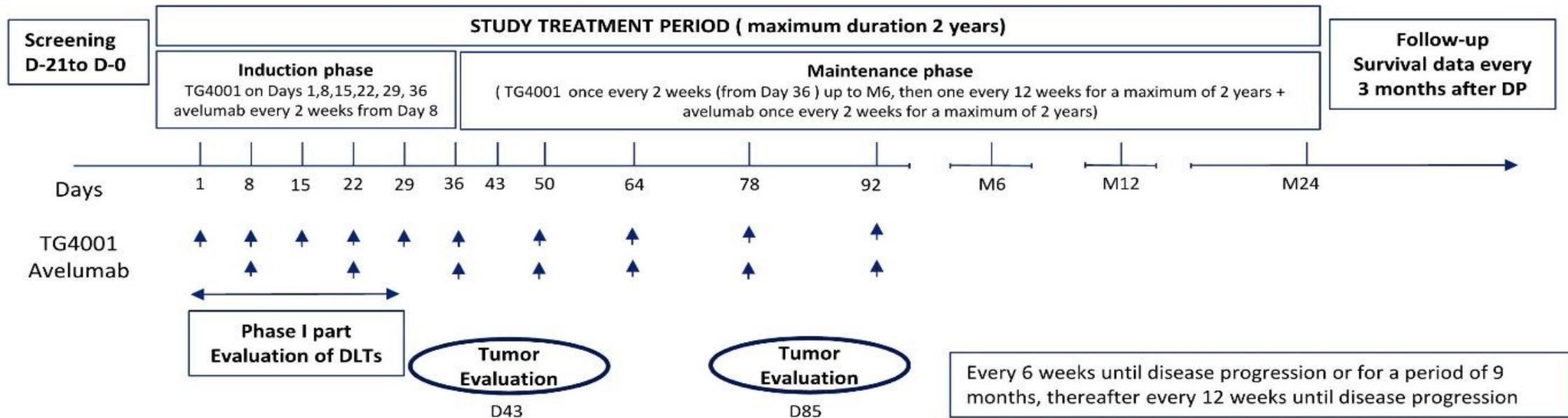
ORR (PhIb), PFS, OS, DoR, DCR, Safety profile (PhII)

Up to 50 patients (in EU)

Multi-center, single arm, open label trial

NCT03260023

TG4001 + Avelumab | Administration schedule



- **TG4001:** Recommended dose for Phase 2 = 5×10^7 pfu – administered SC
- **Avelumab:** 10mg/kg – administered IV

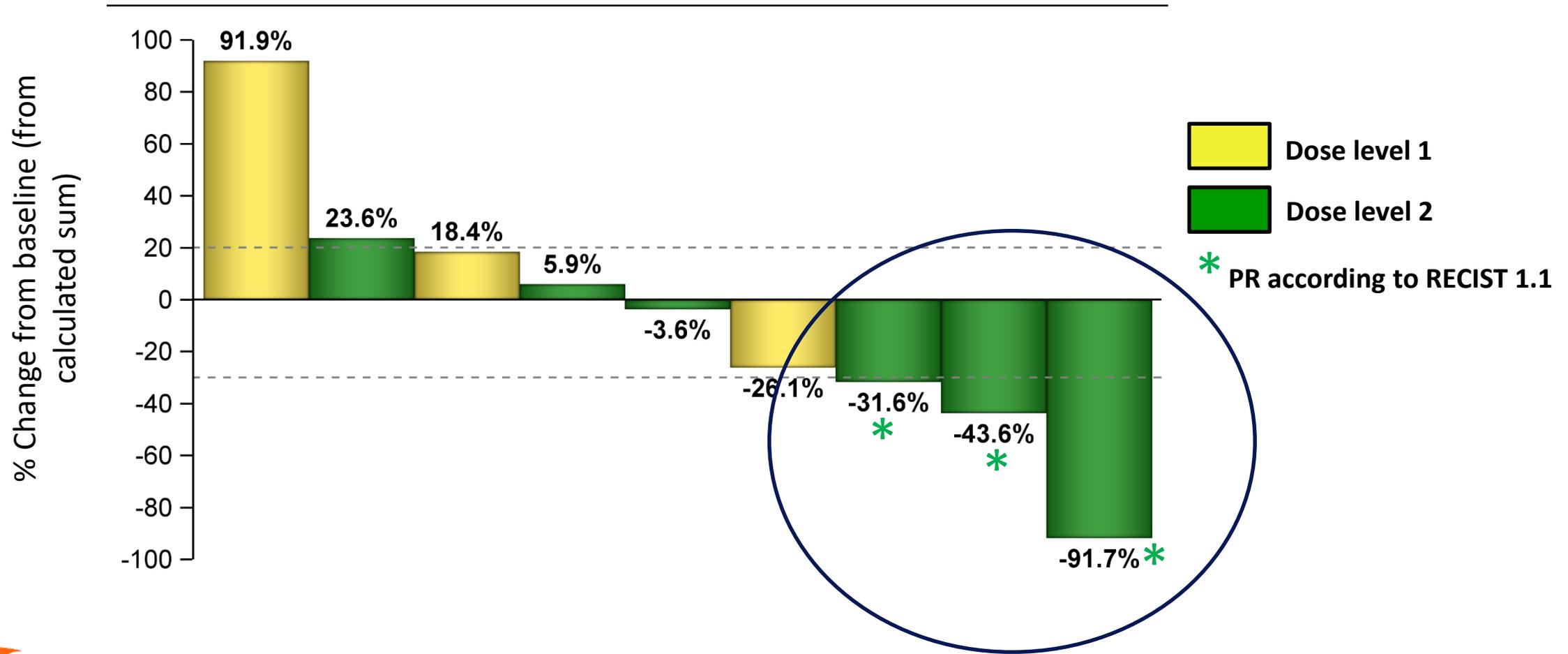
Trial population - Patients with recurrent/metastatic (R/M) HPV16+ cancers

		DL1	DL2	Overall
		5 x 10⁶ pfu	5 x 10⁷ pfu	
		(n=3)	(n=6)	(n=9)
Age (years)	Mean	51.0	61.2	57.8
	Range	45 – 56	39 – 78	39 – 78
Gender	Female	2 (66.7%)	2 (33.3%)	4 (44.4%)
	Male	1 (33.3%)	4 (66.7%)	5 (55.6%)
Performance Status (ECOG)	0	0 (0.0%)	4 (66.7%)	4 (44.4%)
	1	3 (100.0%)	2 (33.3%)	5 (55.6%)
Primary tumor	Anal	2 (66.7%)	0 (0.0%)	2 (22.2%)
	Cervical	0 (0.0%)	1 (16.7%)	1 (11.1%)
	Oropharyngeal	1 (33.3%)	4 (66.7%)	5 (55.6%)
	Vaginal	0 (0.0%)	1 (16.7%)	1 (11.1%)
Histology	Adenocarcinoma	0 (0.0%)	1 (16.7%)	1 (11.1%)
	Squamous cell carcinoma	3 (100.0%)	5 (83.3%)	8 (88.9%)
Number of prior CT lines	Median	3.0	1.5	2.0
	Range	2 – 3	1 – 2	1 – 3
Locoregional relapse		1 (33.3%)	2 (33.3%)	3 (33.3%)
Distant Metastases		3 (100.0%)	6 (100.0%)	9 (100.0%)

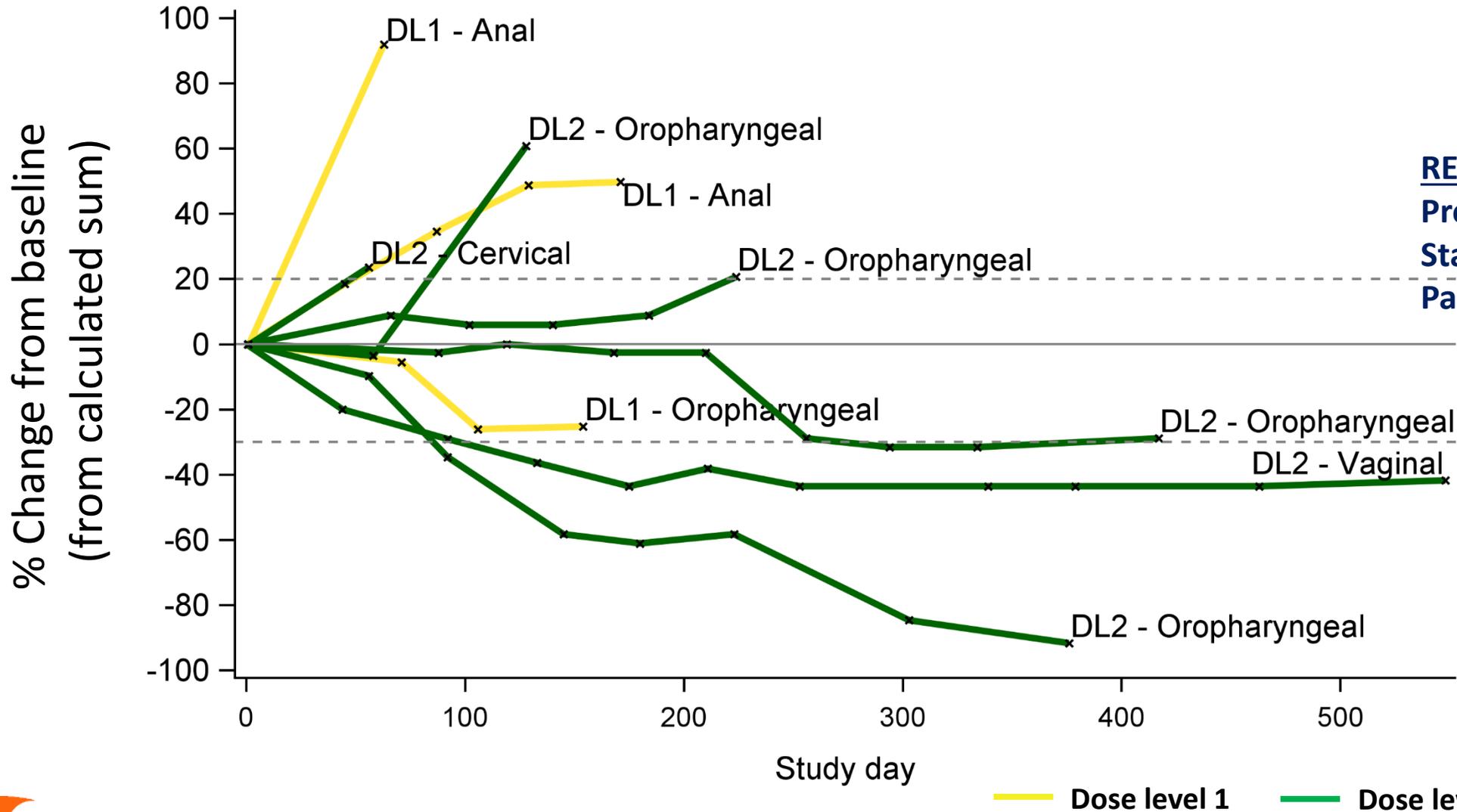
Heavily pretreated patients

100% with distant metastases

Best change in tumor size – 3 partial responses



Individual patient data – 3 durable responses



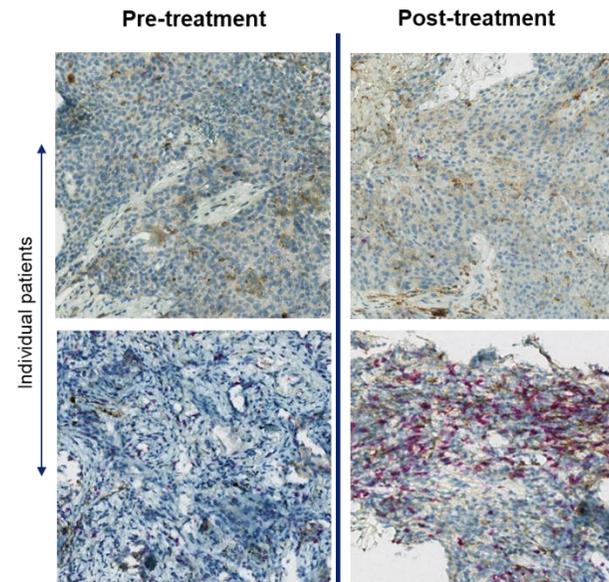
RECIST 1.1 evaluation:
Progression of the disease: 3
Stable disease: 3
Partial response: 3

TG4001 + Avelumab changes the immuno profile of the tumor

➔ The combination regimen induces increased PDL1 expression

Primary Cancer	Time point	% of PD-L1+ tumor cells
vaginal	Baseline Biopsy	35
	Day 43 Biopsy	NA
anal	Baseline Biopsy	50
	Day 43 Biopsy	40
anal	Baseline Biopsy	0
	Day 43 Biopsy	NA
Oropharyngeal	Baseline Biopsy	80
	Day 43 Biopsy	90
	Day 85 Biopsy	80
Cervical	Baseline Biopsy	40
	Day 43 Biopsy	80
Oropharyngeal	Baseline Biopsy	15-20
	Day 43 Biopsy	35
Oropharyngeal	Baseline Biopsy	20
	Day 43 Biopsy	40

➔ Increased PD-L1 expression and CD8 infiltrate



Pink: CD8 staining, Brown PD-L1 staining

Good tolerability profile of TG4001 + Avelumab

- No treatment-related Serious AE has been observed
- The majority of the reported AEs were mild to moderate (grade 1 - grade 2), only two grade 3 AEs were observed in the same patient of DL1
- Most common AEs are transient (mostly injection site reactions, fever and fatigue)

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- Phase 2 ongoing since October 2018 - Interim analysis planned for 1H 2020
- Future positive results will be critical to define registration strategy

Q&A session



Thanks for your attention

Contact

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