2025 ASCO® ANNUAL MEETING

# Randomized phase I trial of adjuvant personalized cancer vaccine TG4050 in resected, locally advanced HNSCC patients (TG4050.02)

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# Key Takeaway Points

1

**Adjuvant TG4050 personalized vaccination is feasible and safe in locally advanced HPV- resectable HNSCC**

2

**TG4050 improves DFS with no recurrences in the vaccinated arm after a median follow-up of 30 months**

3

**TG4050 induces neoantigen-specific CD8 T cell responses that persist after the end of treatment**

# Background

- **Standard of care for locally advanced HNSCC:**
  - Unresectable disease or organ-sparing: radiotherapy +/- chemotherapy
  - Resectable disease: surgery followed by radiotherapy +/- chemotherapy
- **Immunotherapy targeting PD1 is becoming standard of care in resectable disease:**
  - Neoadjuvant and adjuvant Pembrolizumab (KN-689 trial)
  - Adjuvant Nivolumab (NIVOPOSTOP trial)

Pignon et al. *Radiother Oncol* 2009; Bernier et al. *NEJM* 2004; Cooper et al. *NEJM* 2004; Uppaluri et al. *NEJM* 2025; Atkins et al. *ASCO* 2025; Bourhis et al. *ASCO* 2025

# TG4050

- Viral-based **personalized cancer vaccine** using Modified Vaccinia Virus Ankara
- Specifically manufactured for a given patient based on the identification of **specific somatic mutations** using tumor sequencing
- Contains **up to 30 MHC class I and II predicted patient-specific neoantigen epitopes**
- Expected to induce tumor antigen-specific **T cell responses**

Bendjama & Quemeneur *Hum Vaccin Immunother* 2017

# Study design (NCT04183166)

**Key objectives:**
- **Primary:** Safety
- **Secondary:** Feasibility, DFS
- **Exploratory:** Neoantigen specific response

**Selection criteria #1:**
- Resectable HNSCC from oral cavity, oropharynx, larynx, hypopharynx
- HPV negative
- Stage III or IV

**Selection criteria #2:**
- Pathological stage III or IV
- Adjuvant therapy completed
- Disease-free @3 months post adjuvant therapy

Surgery → (chemo)radiation → 3 months → Disease Assessment → R 1:1

**Vaccine manufacturing**

**Arm A:**
- **Adjuvant TG4050**
- TG4050 could be given at recurrence

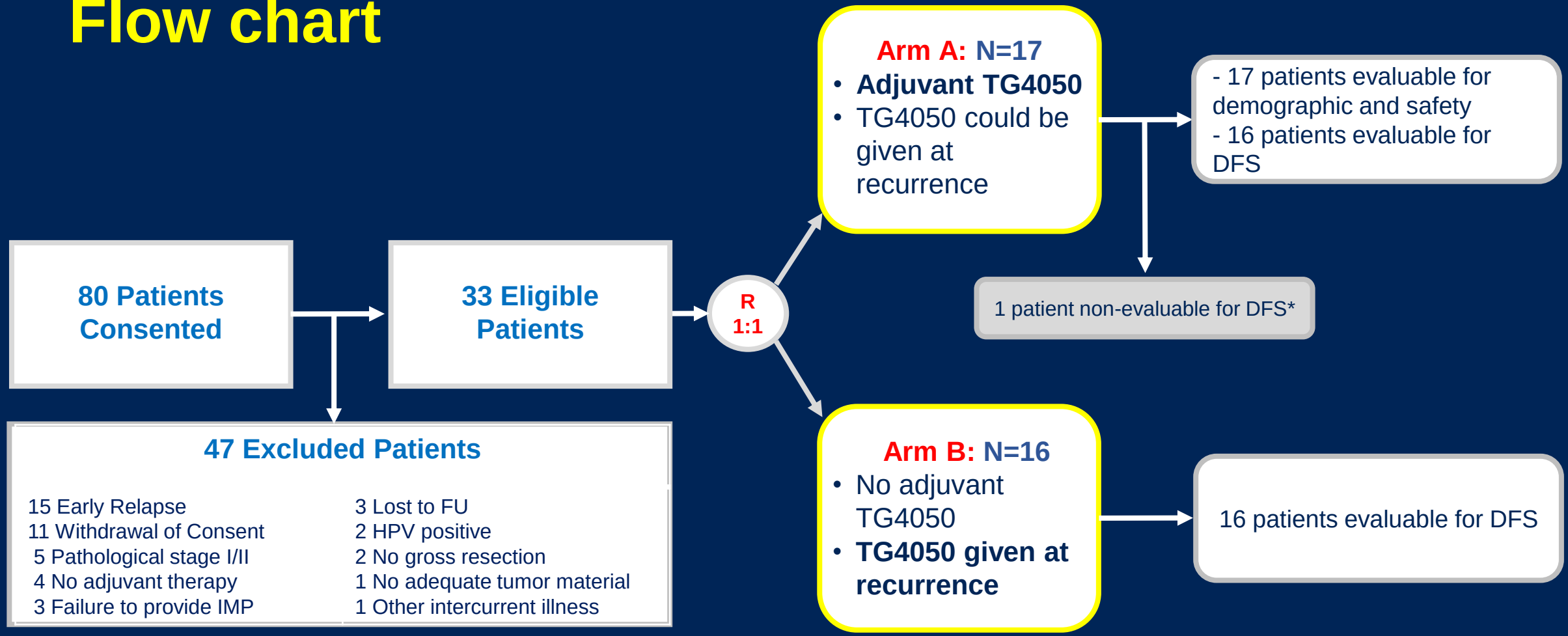
**6 injections qw followed by 14 injections q3w SC**

**Arm B:**
- No adjuvant TG4050
- **TG4050 given at recurrence**

**Stratification factors:**
- Cisplatin (yes/no)
- Pathological stage (III/IV)
- Center


PRESENTED BY: Christophe Le Tourneau, MD, PhD

# Flow chart




* **Minimum exposure not met:** Patient was diagnosed with locoregional recurrence after only 2 administrations of TG4050

# Populations definition for statistical considerations

| Population | Definition per protocol | Primary dataset | Total number of patients (A/B) |
|---|---|---|---|
| **Full analysis set** (FAS) | All randomized patients | Demographic and baseline characteristics | **N=33** (17/16) |
| **Safety population** (SAF) | All randomized patients who received **at least one injection** of TG4050 | Safety analysis | **N=19** (17/2) |
| **Per protocol** (PP) | Minimum exposure before recurrence:<br>Arm A: patients who **completed their 6 weekly injections** of TG4050<br>Arm B: patients who **completed their 6 weeks FU** | DFS | **N=32** (16/16) |

# Patient characteristics

| | Arm A (N=17) | Arm B (N=16) |
|---|---|---|
| **Male / Female, n (%)** | 11 (65%) / 6 (35%) | 13 (81%) / 3 (19%) |
| **Age (years), median (range)** | 61 (26 – 79) | 57 (47 – 74) |
| **ECOG PS 0 / 1, n (%)** | 12 (71%) / 5 (29%) | 9 (56%) / 7 (44%) |
| **Primary tumor location** | | |
| Oral cavity | 14 (82%) | 10 (63%) |
| Oropharynx | 2 (12%) | 2 (13%) |
| Hypopharynx | 1 (6%) | 3 (19%) |
| Larynx | - | 1 (6%) |
| **Clinical stage, n (%)** | | |
| III | 7 (41%) | 3 (20%) |
| IVa | 10 (59%) | 13 (81%) |
| **Pathological stage, n (%)** | | |
| I/II* | 1 (6%) | 1 (6%) |
| III | 4 (24%) | 3 (19%) |
| IVa | 7 (41%) | 5 (31%) |
| IVb | 5 (29%) | 7 (44%) |
| **Concomitant cisplatin, n (%)** | 10 (59%) | 9 (56%) |

* The protocol was further amended to only include Pathological stage III and IV disease

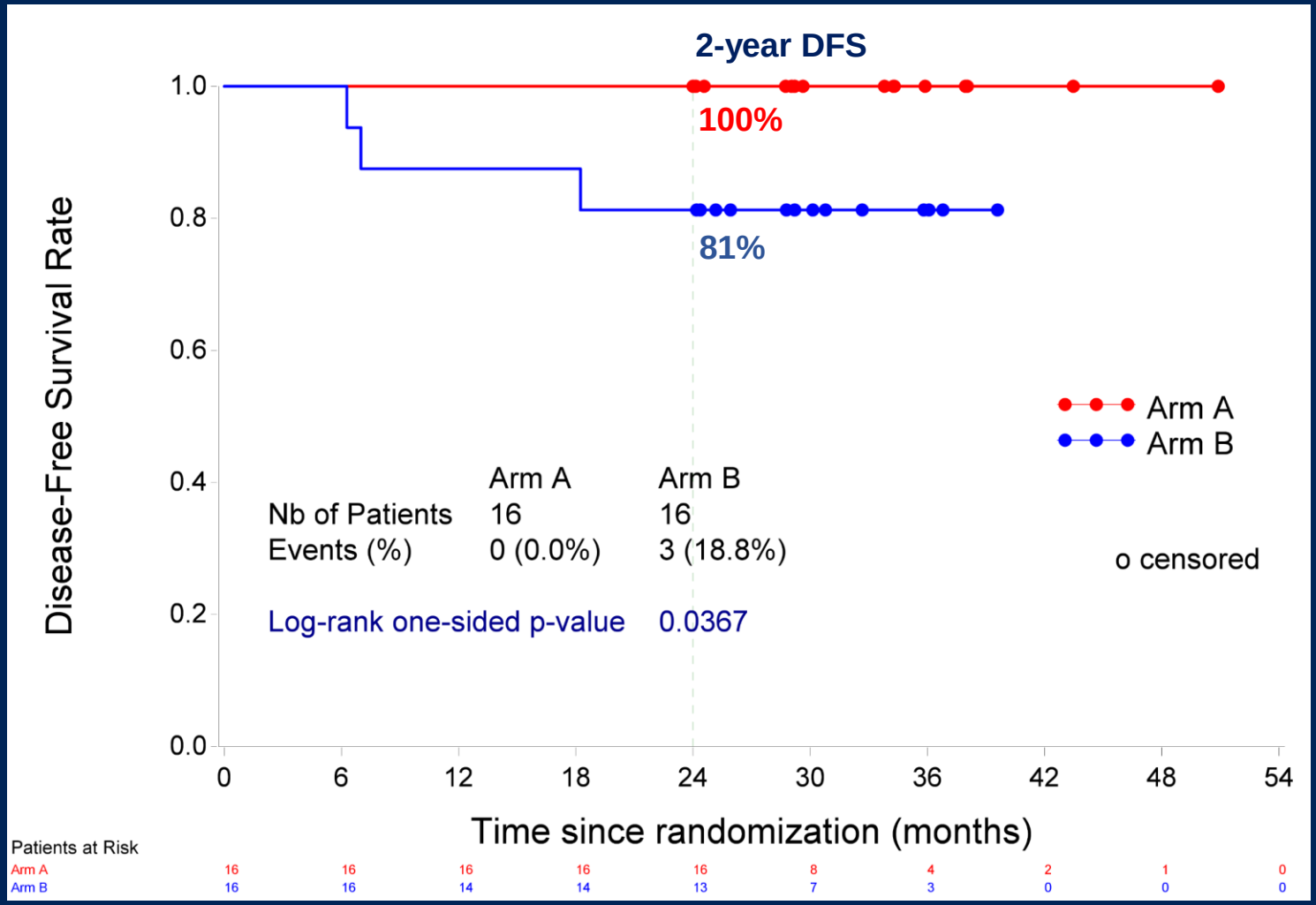
# Pathological risk factors

| | Arm A (N=17) | Arm B (N=16) |
|---|---|---|
| **Extracapsular effraction, n (%)** | 5 (29%) | 8 (50%) |
| **Invaded margins, n (%)** | 4 (24%) | 3 (19%) |
| **Perineural infiltration, n (%)** | 13 (77%) | 7 (44%) |
| **4+ invaded lymph nodes, n (%)** | 2 (12%) | 3 (19%) |
| **No. of risk factors, n (%)** | | |
| 0 | 3 (18%) | 2 (13%) |
| 1 | 5 (29%) | 9 (56%) |
| 2+ | 9 (53%) | 5 (31%) |

# Safety

| | Adjuvant TG4050 (N=17) | TG4050 at recurrence (N=3) |
|---|---|---|
| **Patients with at least one AE related to TG4050, n (%)** | 16 (94%) | 2 (67%) |
| Dose-limiting toxicity | 0 | 0 |
| SAE | 0 | 0 |
| Grade 3-5 AEs | 0 | 0 |
| **Grade 1/2 AEs related to TG4050** | | |
| Injection site reaction | 16 (94%) | 1 (33%) |
| Rash | 2 (12%) | 0 |
| Fatigue | 2 (12%) | 0 |
| Influenza-like syndrom | 2 (12%) | 0 |
| Diarrhoea | 2 (12%) | 0 |
| Lymphopenia | 0 | 1 (33%) |
| Headache | 1 (6%) | 0 |
| Alkaline phosphatase increase | 0 | 1 (33%) |

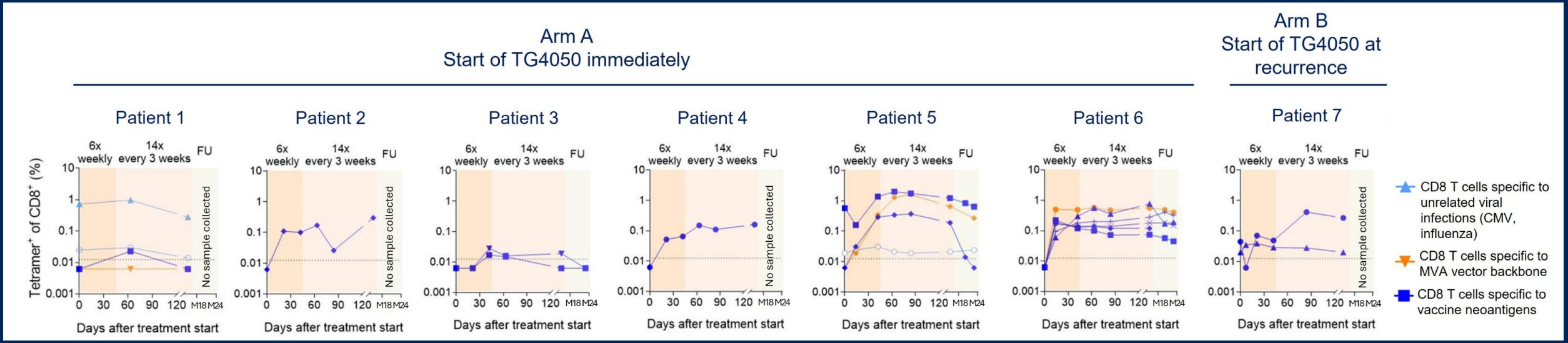
# Efficacy




**Median FU of 30 months**

# Immune response

- **Neoantigen-specific CD8 T cell responses** to multiple vaccine epitopes in the same patient with no evidence of antigen **immunodominance**
- **Persistence** of CD8 T cell responses over 1 year after the end of the treatment



# Conclusions

**Adjuvant personalized vaccination with TG4050 is feasible and safe in resectable HPV- locally advanced HNSCC patients, and induces long-lasting immune responses to vaccine neoantigens**

**Adjuvant personalized vaccination with TG4050 improves DFS with no recurrences in the vaccinated arm, supporting the ongoing randomized phase II part of the trial**
(last randomization expected for Q4 2025)

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